Endometrial Cancer

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2.1 Anatomy, Histology, and Physiology

The uterus is the most common site of cancer in the female genital tract [1, 2]. Most uterine cancers in the United States arise from the endometrium, which is the innermost layer of the uterine corpus and constitutes the lining of the uterine cavity (Table 2.1). The endometrium is an integral component of the female reproductive system, undergoing cyclic changes in response to intricate variations in circulating levels of sex hormones, which ultimately result in the development of a local environment optimal for the implantation and subsequent development of an embryo (Table 2.2). Shifting trends with an apparent increase in incidence of endometrial cancer across the world probably reflect changes in the prevalence of established risk factors, namely obesity, low parity, late menarche, early menopause, and increasing age [3]. Most patients present at an older age than patients with cervical cancer. The typical clinical scenario is vaginal bleeding in a postmenopausal female. Prognosis depends on a number of factors: the most important is the depth of myometrial invasion by tumor, but other factors include stage, lymphovascular invasion, histologic grade, and lymph node status. If detected at an early stage, endometrial cancer is potentially curable [4]. Diagnosis is made on the basis of clinical suspicion with pathological confirmation from transvaginal biopsy or curettage of the endometrial cavity. Imaging has little role in the diagnosis of the primary tumor, but it is helpful for staging newly diagnosed cancer and detecting recurrence following endometrial cancer treatment (Table 2.3).

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Table 2.1 Uterine zonal anatomy and histology

Layer	Histology	Features relevant to imaging
Endometrium	Single-layer columnar epithelium resting on a layer of connective tissue that varies in thickness throughout the menstrual cycle	Thickness varies throughout menstrual cycle (thinnest just after menstruation and gradual thickening over the cycle)
Myometrium	Smooth muscle layer; the innermost aspect, the "junctional zone," constitutes the interface between the myometrium and endometrium	May appear indistinct or shrink during menstruation; the junctional zone may thicken (paralleling changes in endometrial thickness, but to a lesser degree) and mimic uterine pathology (e.g., adenomyosis)
Perimetrium	Serosal layer covering the dorsal and ventral aspects of the uterus	

Table 2.2 Factors affecting endometrial thickness

Factor	Comments
Physiologic	In premenopausal women, endometrial cavity is thinnest just after menstruation and gradually thickens over the menstrual cycle
Hormone replacement therapy	Biopsy is warranted if endometrial thickness is >8 mm if the patient is asymptomatic or ≥5 mm in the presence of postmenopausal bleeding
Endometrial hyperplasia/polyp	Imaging cannot differentiate endometrial hyperplasia or polyps from stage IA endometrial cancer; the most helpful feature to exclude cancer is the absence of myometrial or cervical invasion

Table 2.3 Imaging techniques used for evaluation of the endometrium

Technique	Main use	Advantages	Disadvantages
Ultrasound	First-line evaluation of uterine pathology	Readily available Cost-effective Usually well tolerated	Operator-dependent Limited accuracy in staging endometrial cancer
CT	Staging of endometrial cancer	Fast Reproducible More widely available than MRI	Involves ionizing radiation Contrast resolution is not as good as ultrasound or MRI
MRI	Most accurate for local staging (*e.g.*, depth of myometrial invasion) and evaluation of recurrence	Superb contrast resolution No ionizing radiation	More expensive and less readily available than ultrasound or CT
Positron emission tomography (PET)	Evaluation of metastatic disease	Depicts both anatomy and function Whole-body evaluation	Radiation from both CT and PET component of the examination

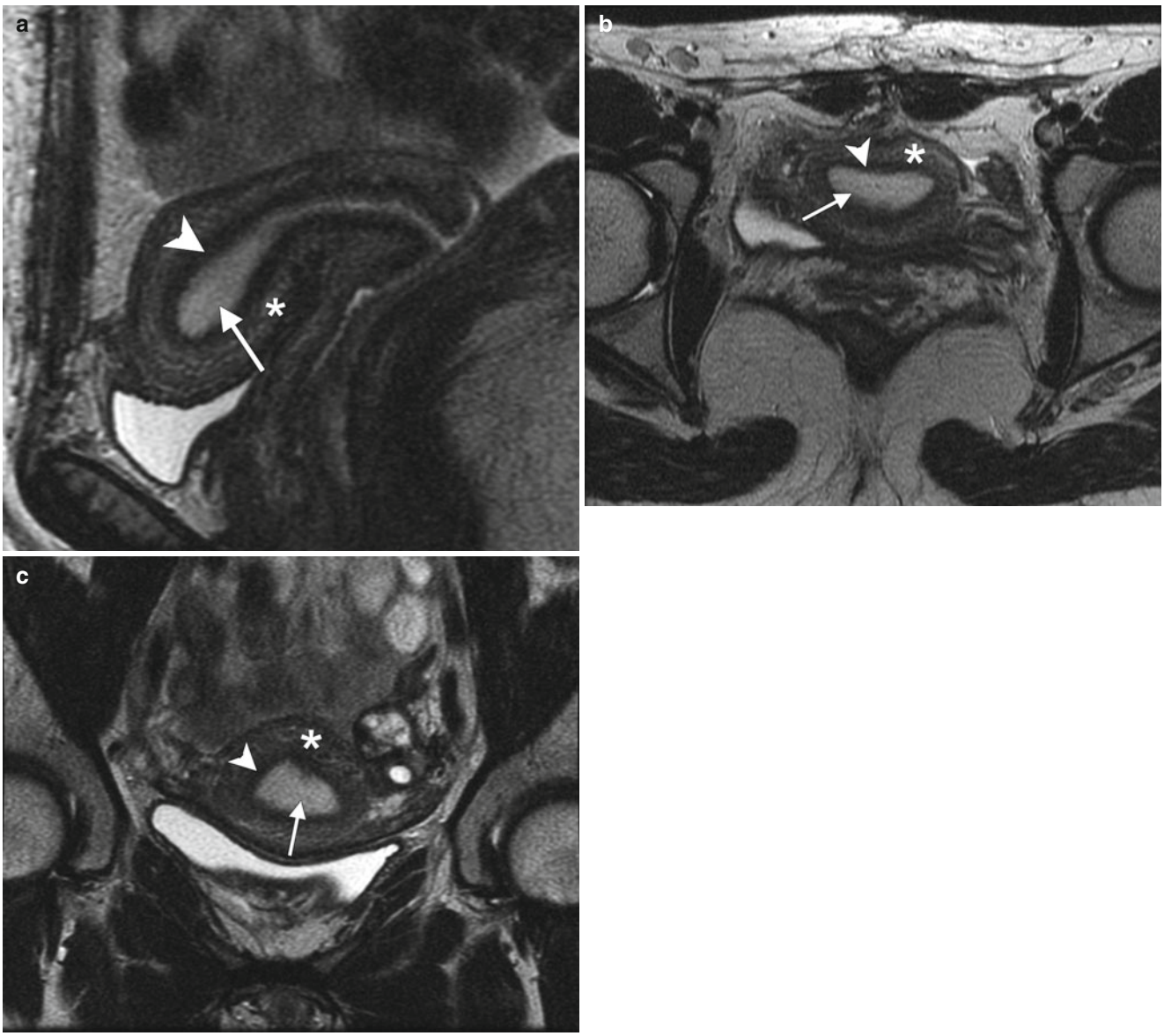


Fig. 2.1 Zonal anatomy of the normal uterus. T2-weighted sagittal (**a**), axial (**b**), and coronal (**c**) images demonstrate the normal uterine zonal anatomy in a premenopausal woman, including the endometrium (*arrows*), junctional zone (*arrowheads*), and outer myometrium (*asterisks*)

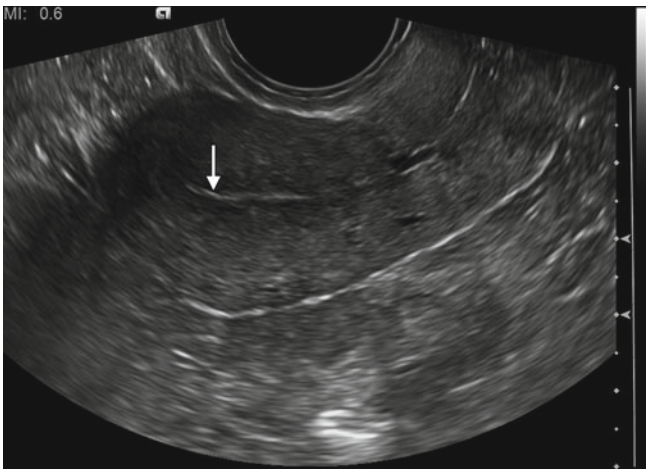


Fig. 2.2 Longitudinal 2-D transvaginal ultrasound image of the normal endometrium (*arrow*). The hallmark of endometrial cancer on imaging is thickening of the endometrial cavity. Varying size cutoffs have been proposed: the prevalence of endometrial cancer has been reported to be 0.6 % when the endometrial thickness is <5 mm, compared with 19 % when the endometrial thickness is 5 mm or more [5]. However, endometrial thickening may be present in many physiologic and benign conditions

2.2 Benign Uterine Pathology

Benign pathologies to be considered in symptomatic women include adenomyosis, leiomyomata (fibroids), and intravenous leiomyomatosis.

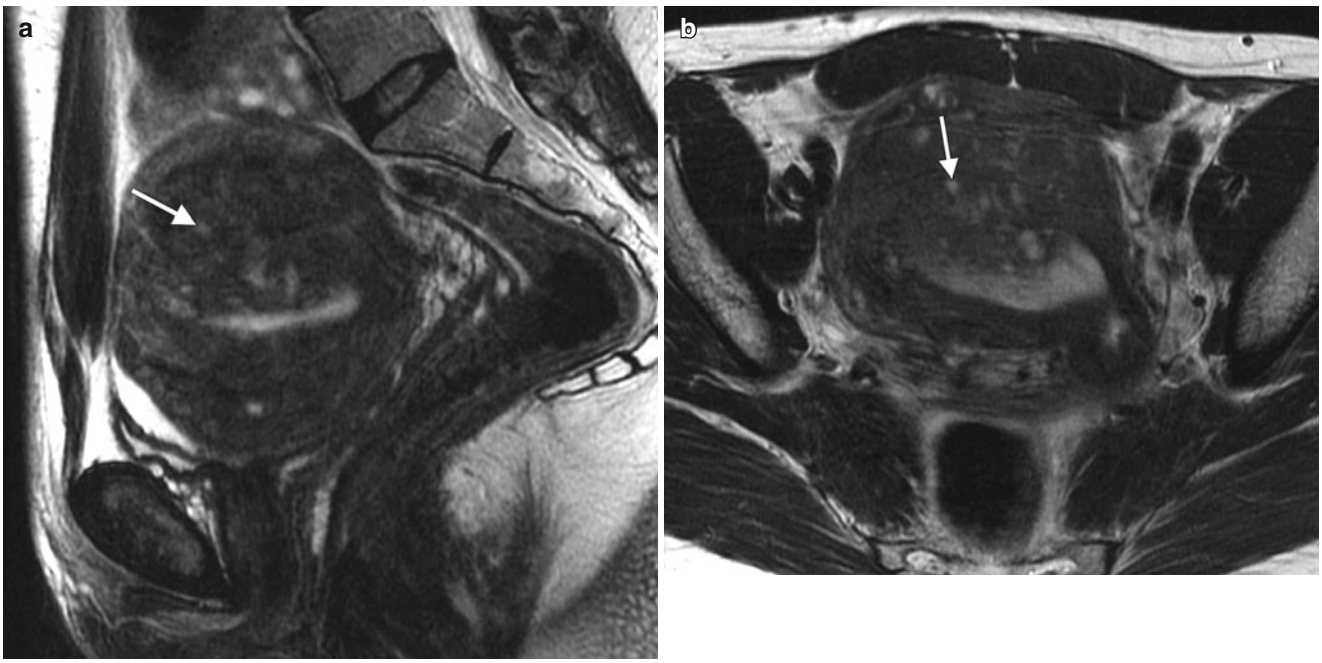


Fig. 2.3 Adenomyosis is the term used for the presence of endometrial glands within the myometrium. The most common imaging findings are thickening of the junctional zone (>12 mm on the midsagittal plane on T2-weighted MRI has an accuracy of 85 % and specificity of 96 % [6]) and the presence of "microcysts" in the myometrium measuring 3–7 mm. *Pitfall*: Physiologic myometrial contractions may simulate the presence of adenomyosis. The use of antiperistaltic medication or repeat imaging a few minutes after the initial acquisition have been proposed as methods to circumvent this issue, as myometrial contractions should subside and adenomyosis persists following such maneuvers. These representative images show a 45-year-old premenopausal woman with severe menstrual cramps and menorrhagia. Sagittal (**a**) and axial (**b**) T2-weighted images demonstrate a thickened junctional zone with multiple punctate cystic spaces (*arrows*) consistent with adenomyosis

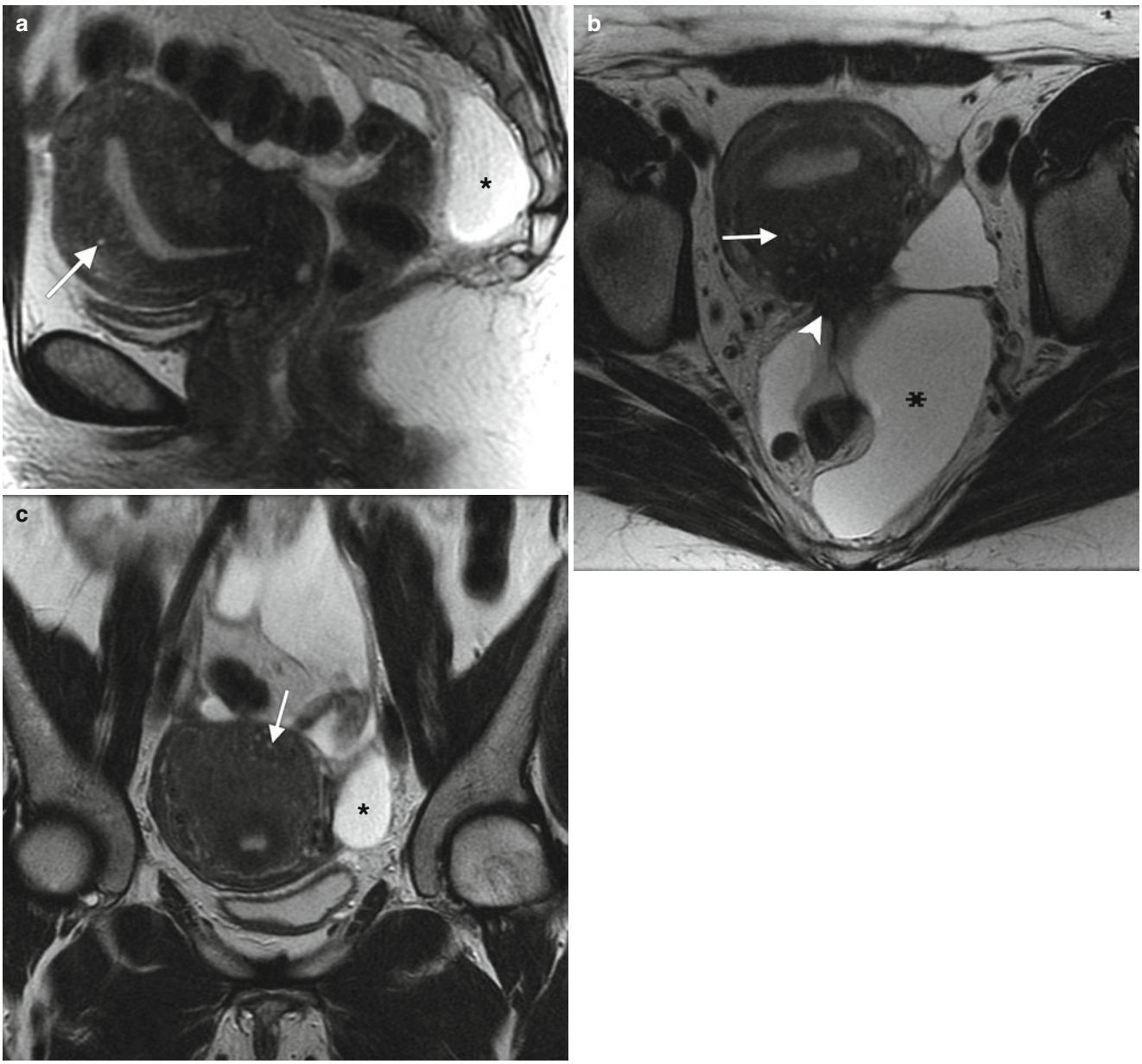


Fig. 2.4 42-year-old woman with a history of appendectomy and myomectomy for dysfunctional uterine bleeding. Sagittal (**a**), axial (**b**), and coronal (**c**) T2-weighted MR images demonstrate thickening of the junctional zone with small T2-hyperintense spaces (*arrows*) consistent with adenomyosis. There is also retraction and tethering of the soft tissues along the posterior uterine wall (*arrowhead*) suspicious for endometriosis. A multiloculated cystic structure (*asterisks*) conforming to the shape of the pelvis probably represents a peritoneal inclusion cyst

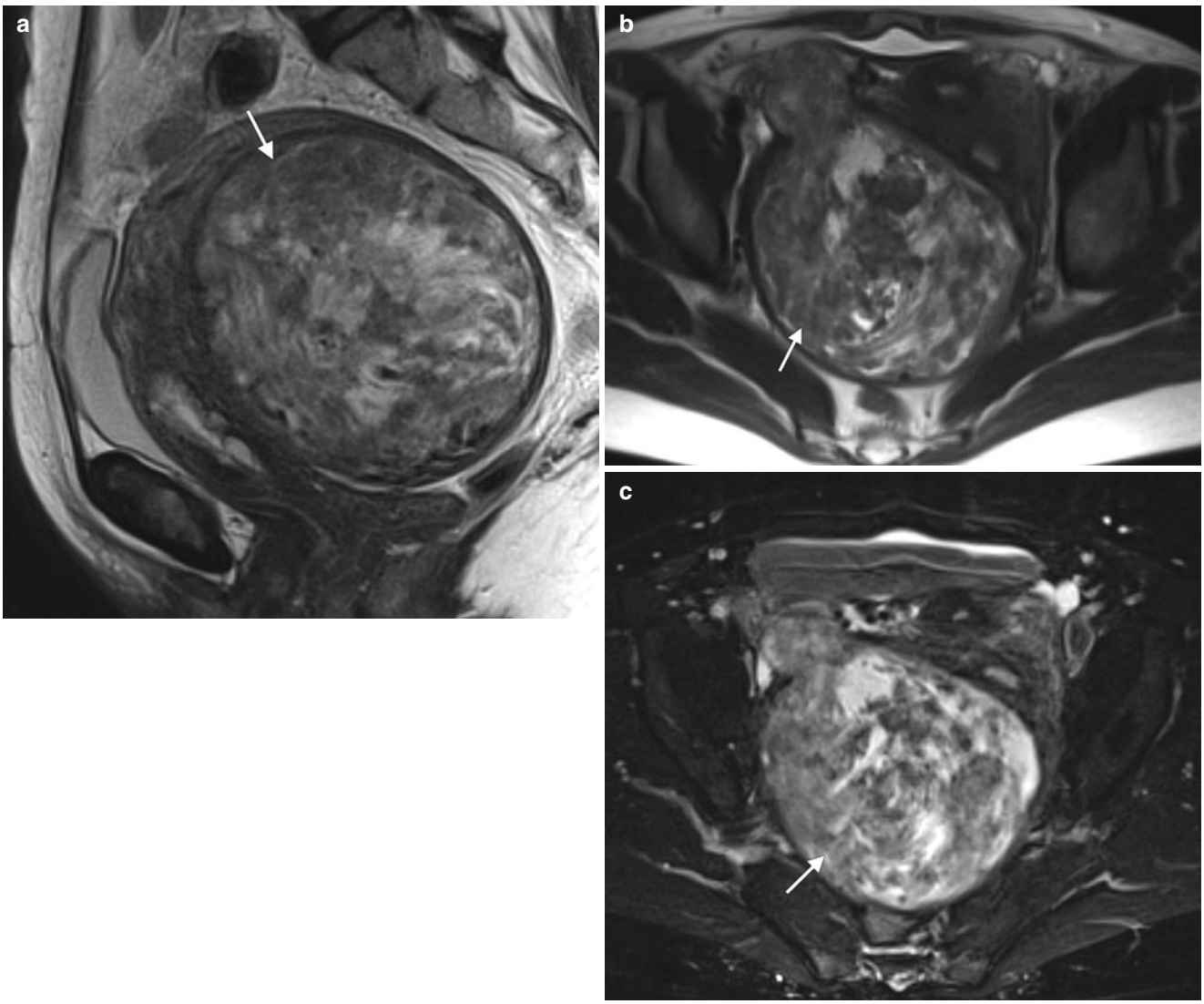


Fig. 2.5 Uterine leiomyomata (fibroids) are the most common tumors in women. They are benign masses originating from the myometrium. Symptoms vary and are related to the size and location of the tumor. The most common symptoms are menorrhagia, pelvic pressure (pain, increased urinary frequency), and infertility. These representative MR images are from a 51-year-old woman with pelvic pressure and dyspareunia. Sagittal (**a**) and axial (**b**) T2-weighted images and fat-suppressed T1-weighted images following the intravenous administration of gadolinium (**c**) demonstrate a heterogeneously enhancing myometrial mass (*arrows*). The patient underwent a hysterectomy for symptom control. Pathology confirmed the diagnosis of uterine leiomyoma

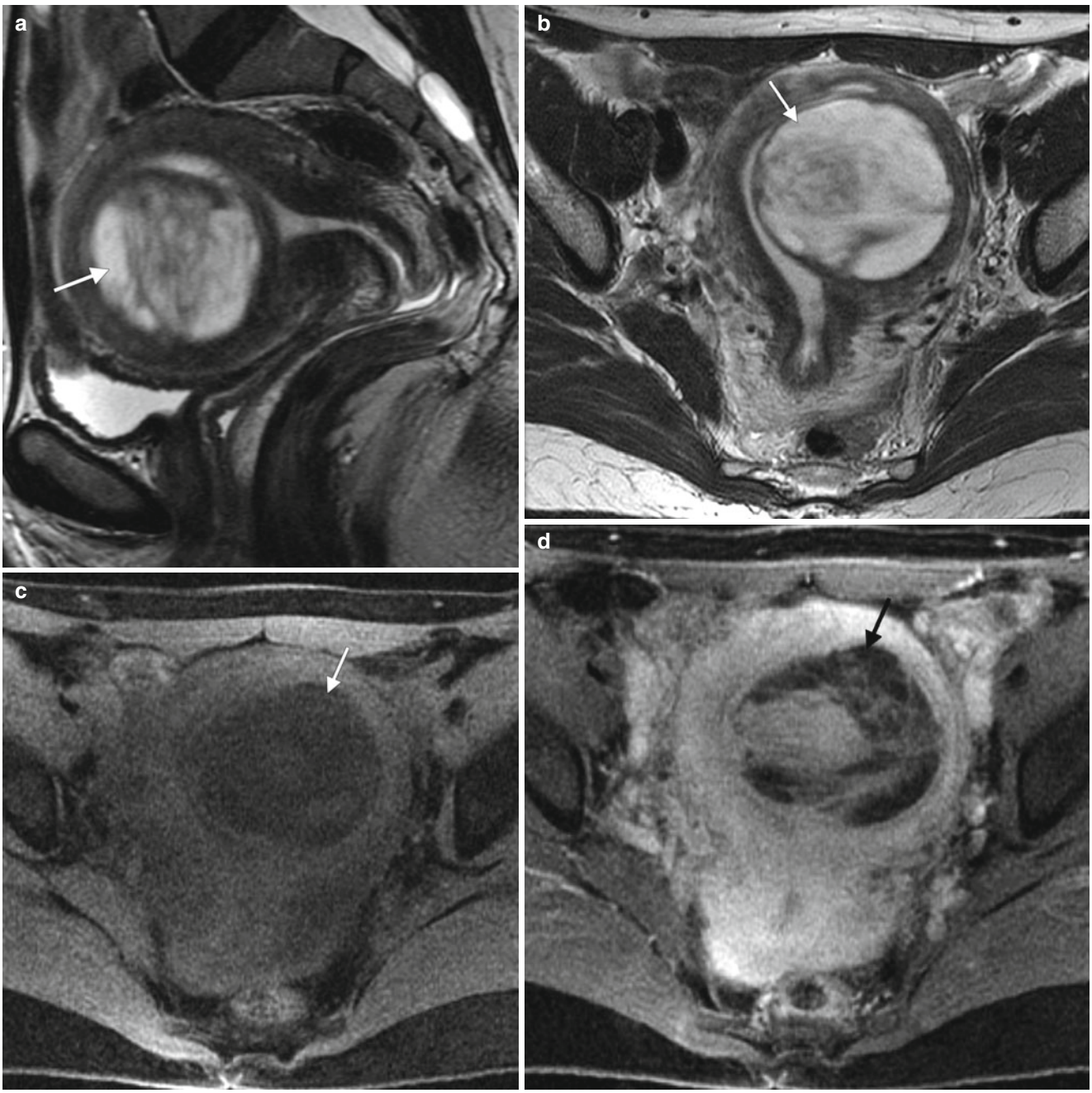


Fig. 2.6 The appearance of uterine leiomyomas is variable. These images show a 44-year-old woman with worsening menometrorrhagia over 3 years. Sagittal (**a**) and axial (**b**) T2-weighted MR images and axial fat-suppressed T1-weighted images before intravenous gadolinium (**c**) and after gadolinium (**d**) demonstrate a predominantly cystic, well-circumscribed, submucosal myometrial mass in the left uterine body (*arrows*) with enhancing septations. Pathology showed a degenerating leiomyoma with hydropic changes

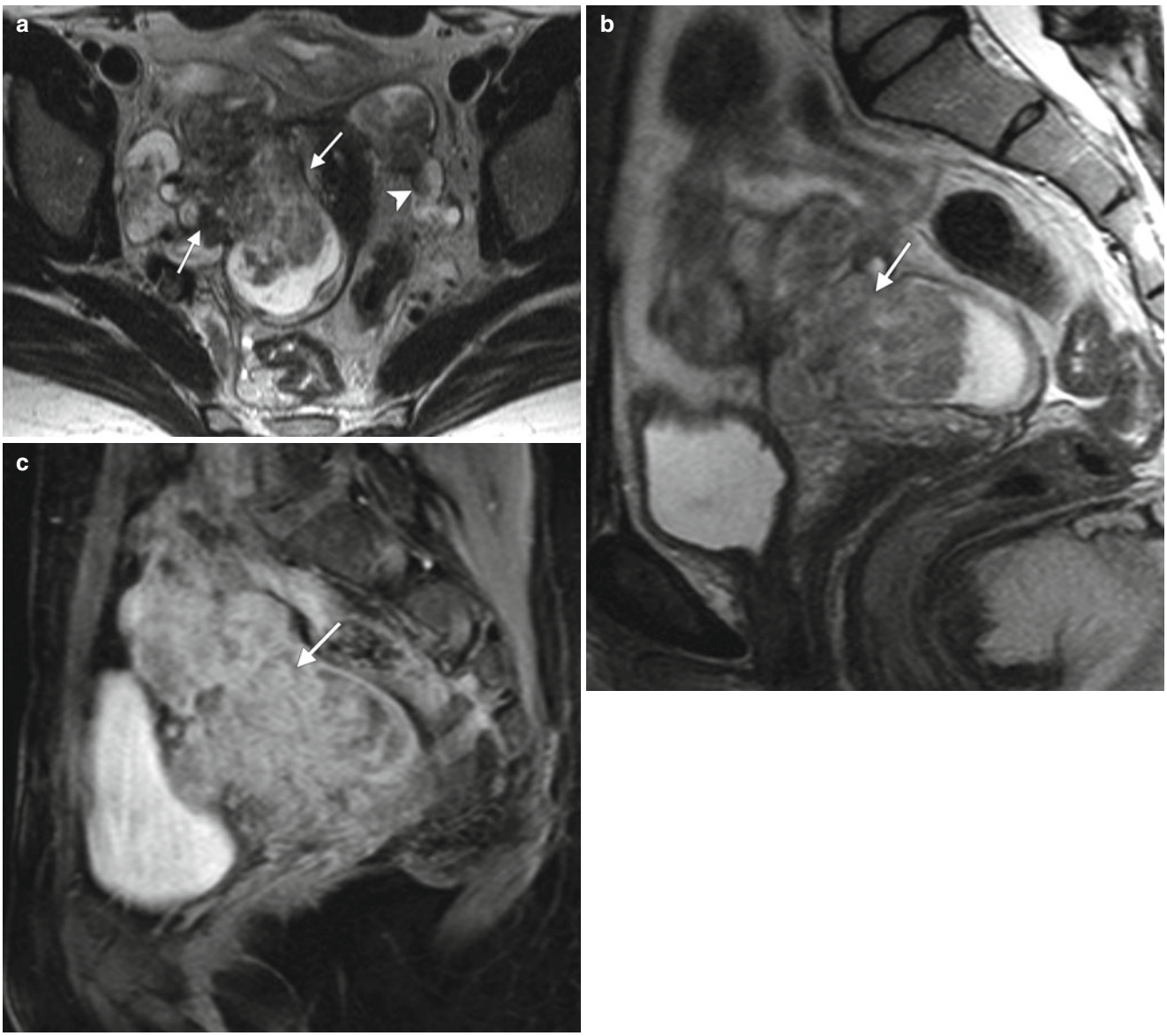


Fig. 2.7 Intravenous leiomyomatosis is a rare form of uterine leiomyomatosis, usually presenting in premenopausal women. It is characterized by intravascular extension of nodular masses composed histologically of benign smooth muscle. Enhancing tumors may extend to uterine, gonadal, and iliac veins, inferior vena cava, and heart and pulmonary vasculature. This pathology is estrogen-dependent, and long-term prognosis is very good after resection. Below are representative images from a 44-year-old woman with multiple previous uterine myomectomies. Axial (**a**) and sagittal (**b**) T2-weighted MR images and a sagittal fat-suppressed, T1-weighted image following intravenous administration of gadolinium (**c**) demonstrate multiple, bilateral, heterogeneously enhancing masses in the pelvis (*arrows*). Coronal (**d**) and sagittal (**e**) contrast-enhanced CT scans demonstrate tumor extension into the right common iliac vein and inferior vena cava (*arrowheads*). Pathology confirmed the diagnosis of benign leiomyomata with intravenous leiomyomatosis

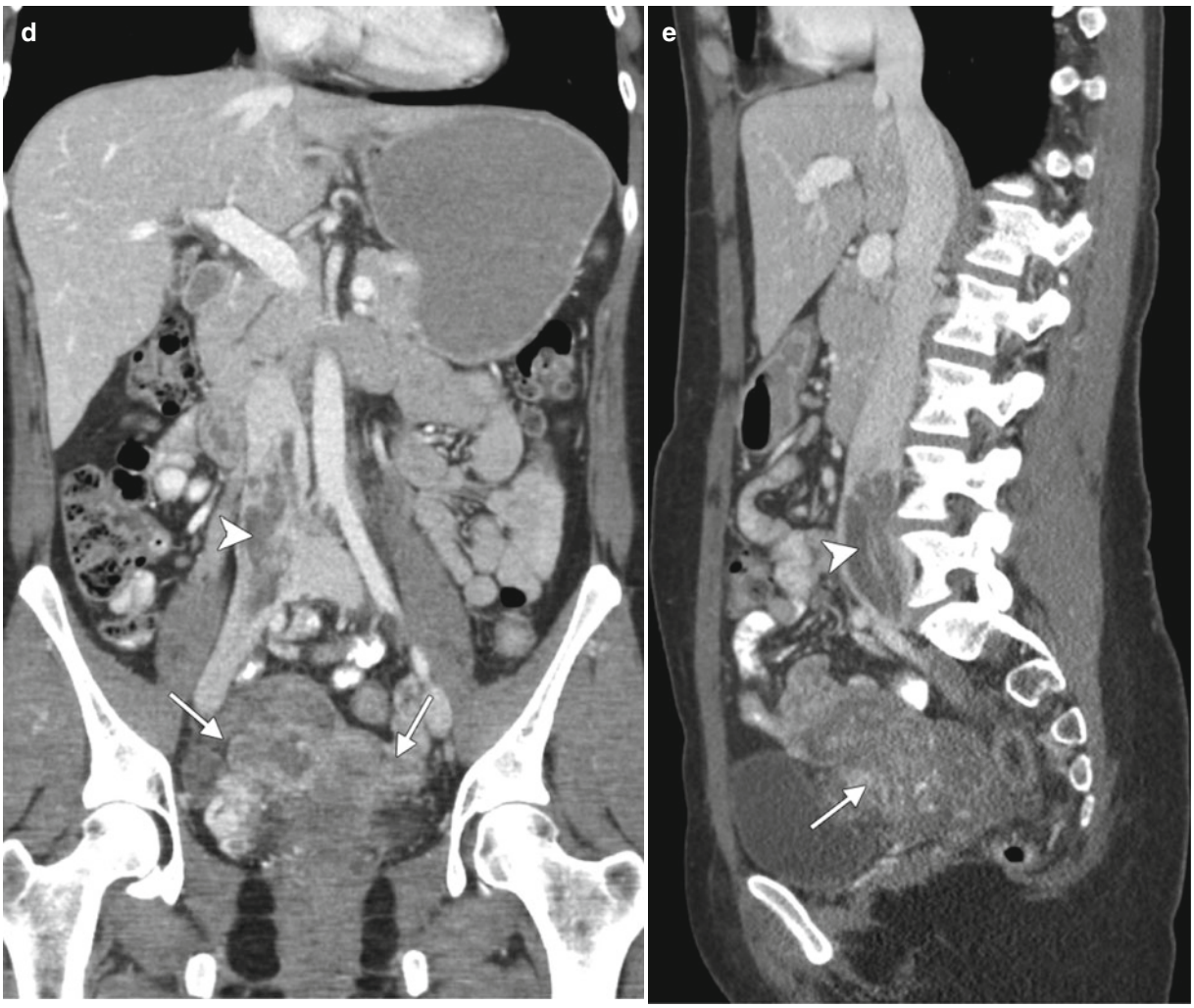


Fig. 2.7 (continued)

2.3 Malignant Uterine Pathology

The histologies of endometrial cancer (Table 2.4) are reflected in changed MRI signal characteristics (Table 2.5). The prognosis is suggested by the staging system of the International Federation of Gynecology and Obstetrics (FIGO) (Tables 2.6 and 2.7). Imaging findings that should be included in the radiology report are presented in Table 2.8.

Table 2.4 Endometrial cancer histologies

Histology	Prevalence (%)
Endometrioid adenocarcinoma	85
Serous adenocarcinoma	10
Clear cell adenocarcinoma	<5
Uterine sarcomas Leiomyosarcoma Endometrial stromal sarcoma Carcinosarcoma (malignant mixed müllerian tumor)	<1

Table 2.5 Typical MRI signal characteristics of endometrial cancer in relation to normal endometrium and normal myometrium

Imaging type	Characteristics of endometrial cancer
Relative to endometrium	
T1WI	Isointensity
T2WI	Intermediate signal intensity
T1WI+C	Earlier enhancement
Relative to myometrium	
T1WI	Variable intensity
T2WI	Hyperintensity
T1WI+C	Less and more delayed enhancement[a]
Diffusion-weighted MRI	Hyperintensity (hypointensity on ADC map)

ADC apparent diffusion coefficient, *T1WI* T1-weighted imaging, *T1WI+C* T1-weighted imaging with contrast enhancement, *T2WI* T2-weighted imaging

[a]Maximum contrast between hyperintense myometrium and hypointense endometrial tumor occurs 50–120 s after contrast medium administration; this is the most important phase for accurate assessment of the depth of myometrial invasion. Delayed-phase images obtained 3–4 min after contrast medium administration are useful in evaluating for cervical stromal invasion (FIGO stage II). The presence of an intact enhancing cervical mucosa excludes stromal invasion

Table 2.6 Endometrial cancer staging, International Federation of Gynecology and Obstetrics (FIGO), 2009

FIGO stage	Description	5-Year overall survival (%) [4]
IA	Tumor confined to the uterus, no or <50 % myometrial invasion	85
IB	Tumor confined to the uterus, ≥50 % myometrial invasion	
II	Cervical stromal invasion	75
IIIA	Tumor invades serosa or adnexa	45
IIIB	Vaginal and/or parametrial involvement	
IIIC1	Pelvic lymph node involvement	
IIIC2	Para-aortic lymph node involvement	
IVA	Tumor invasion of bladder mucosa and/or bowel mucosa	25
IVB	Distant metastases	

Adapted from Pecorelli [7]

Table 2.7 Key changes in the 2009 FIGO Staging System for Endometrial Cancer

FIGO 2009	FIGO 1988
Stage IA: myometrial invasion = none OR < 50 % Stage IB: myometrial invasion ≥50 %	Stage IA: myometrial invasion = none Stage IB: myometrial invasion = <50 % Stage IC: myometrial invasion ≥50 %
Stage II: cervical stromal invasion (without subgrouping in stage IIA or IIB). Tumors with endocervical glandular invasion are considered stage I tumors	Stage IIA: endocervical glandular invasion Stage IIB: cervical stromal invasion
Stage IIIC is divided into: Stage IIIC1: pelvic lymph node involvement Stage IIIC2: para-aortic lymph node involvement	Stage IIIC: any lymphadenopathy (pelvic or retroperitoneal)

FIGO International Federation of Gynecology and Obstetrics.

Table 2.8 Information to include in the radiology report

Finding	Details
Myometrial invasion <50 % vs ≥50 %	Differentiation between no myometrial invasion and <50 % myometrial invasion is not necessary, as it does not affect staging
Cervical stromal and/or vaginal invasion	Present vs absent
Extrauterine extension	Adnexae, bladder, rectum
N stage	Regional nodes: para-aortic, common, internal and external iliac (including obturator) regions
Metastases	Liver and lung most common locations

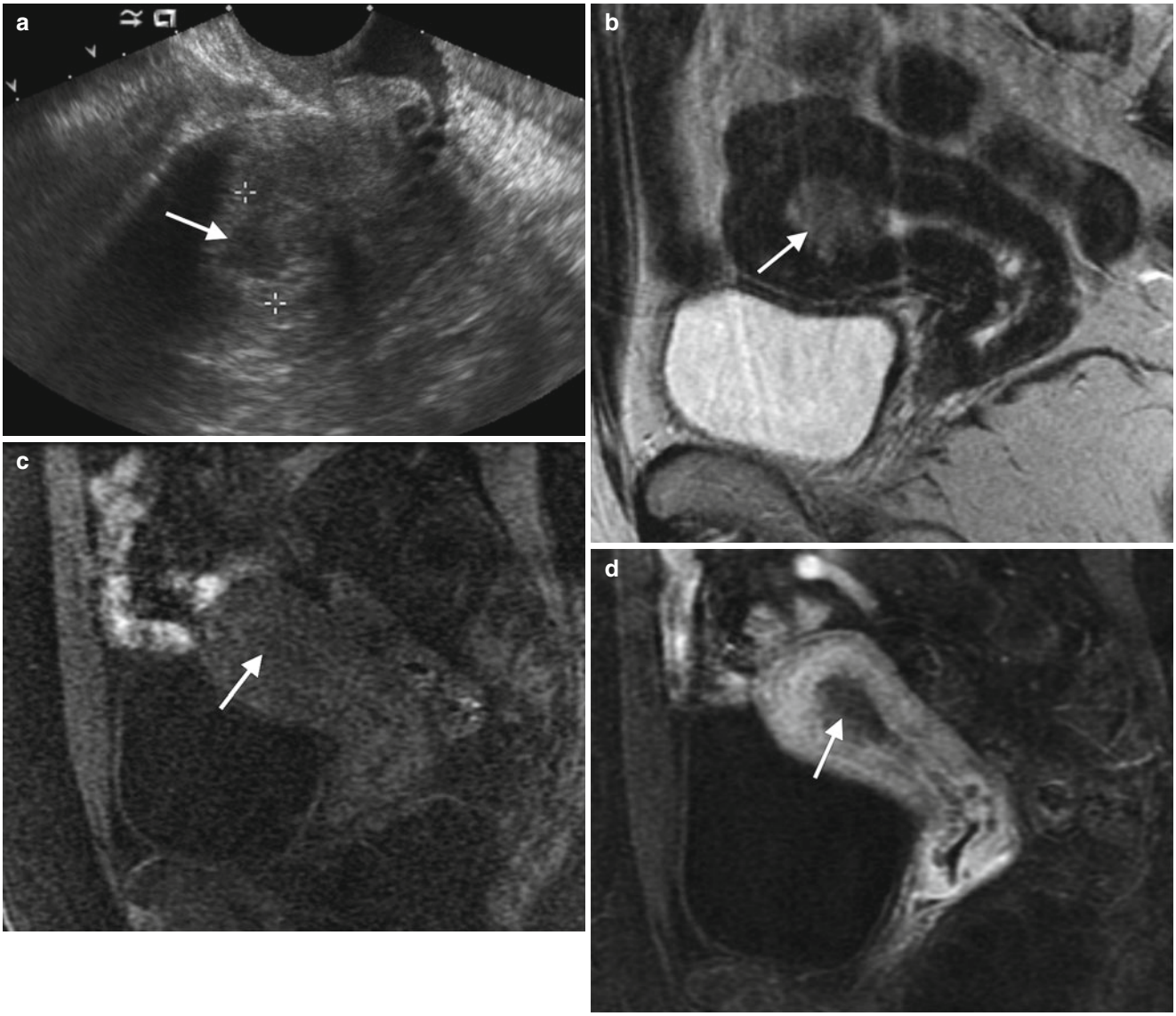


Fig. 2.8 Endometrial thickening is the hallmark of endometrial cancer. This 64-year-old woman with a history of breast cancer underwent a screening gynecologic evaluation, and ultrasound (**a**) revealed a thickened endometrial cavity (20 mm). A sagittal T2-weighted MR image (**b**) and sagittal fat-suppressed T1-weighted images before (**c**) and after (**d**) the administration of intravenous gadolinium revealed a soft tissue endometrial mass with superficial myometrial invasion (*arrows*). Pathology showed an endometrioid adenocarcinoma of the endometrium

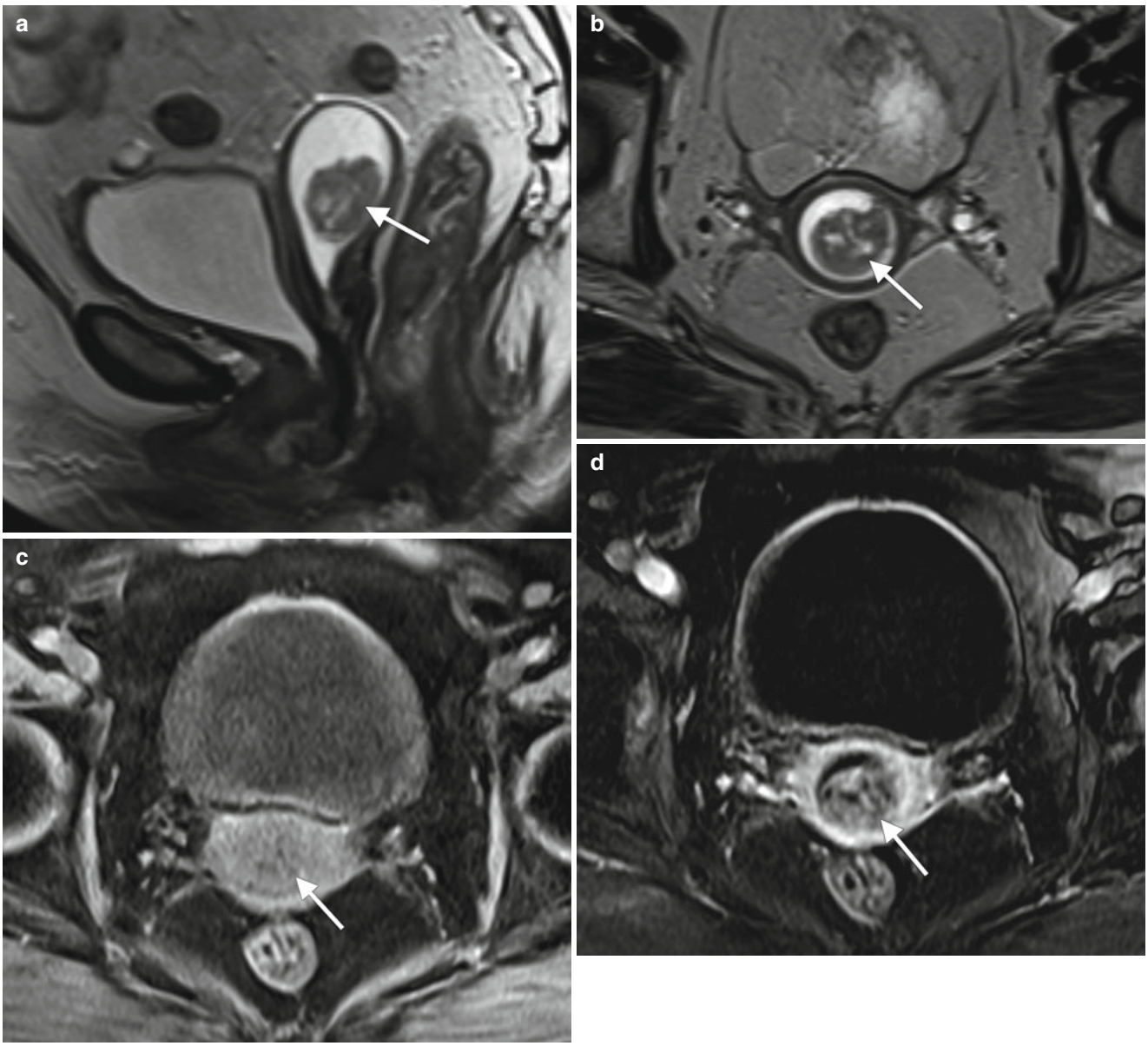
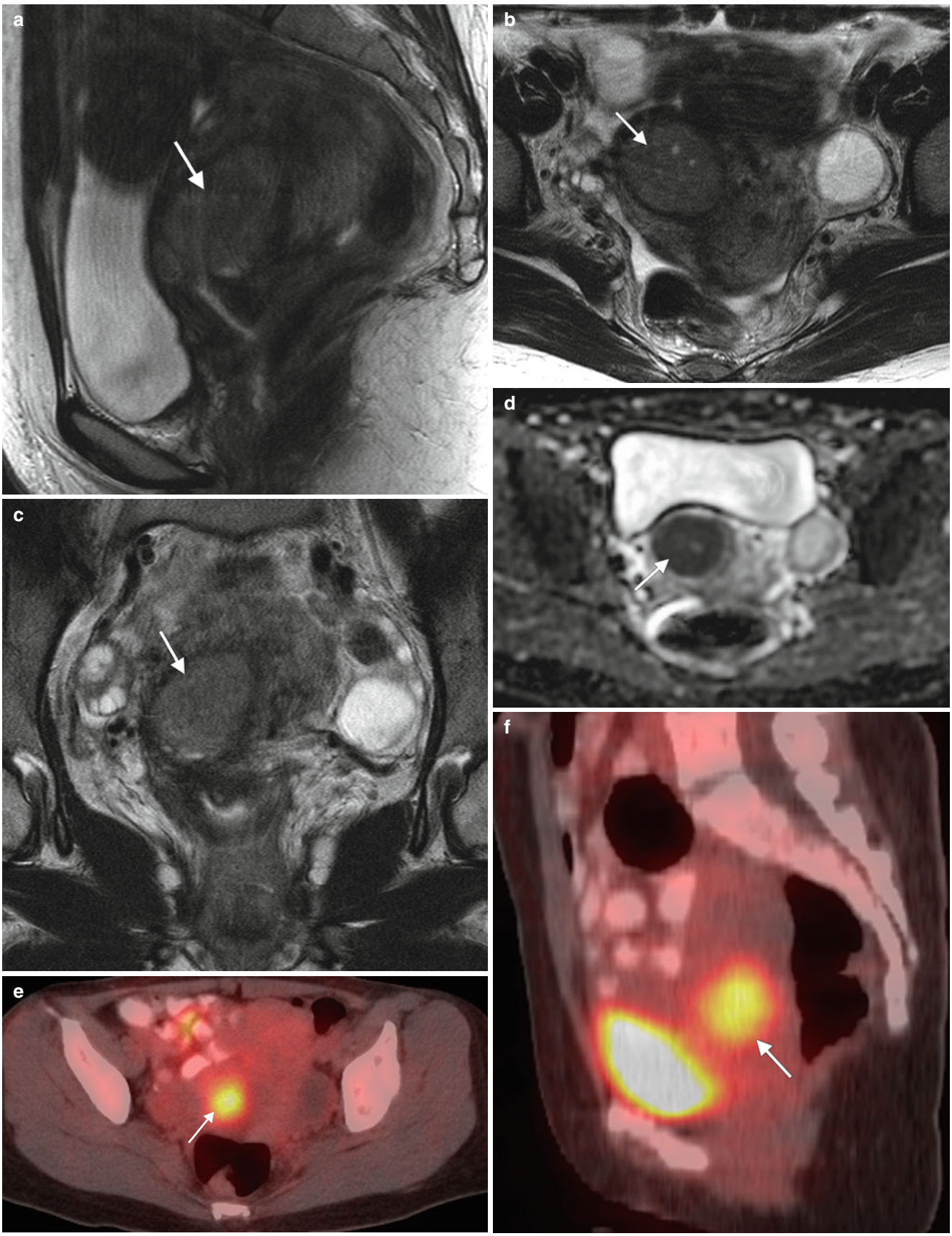


Fig. 2.9 FIGO stage IA endometrial cancer in a 65-year-old postmenopausal patient with vaginal spotting. Sagittal (**a**) and axial (**b**) T2-weighted MR images and axial, fat-suppressed T1-weighted images before (**c**) and after (**d**) intravenous gadolinium demonstrate an enhancing soft tissue endometrial mass (*arrows*) with uninterrupted enhancement of the subendometrial stripe, which indicates absence of myometrial invasion. The endometrial cavity is distended, probably due to cervical stenosis

Fig. 2.10 FIGO stage IA endometrial cancer in a 39-year-old premenopausal woman with menorrhagia. Sagittal (**a**), axial (**b**), and coronal (**c**) T2-weighted MR images, an axial apparent diffusion coefficient map derived from diffusion-weighted MRI (**d**), and fused PET/CT images (**e**, **f**) demonstrate a hypermetabolic soft tissue tumor (*arrows*) expanding the endometrial cavity. The adjacent myometrium is compressed but not invaded. An exophytic leiomyoma is also present (*arrows*). Pathology showed a grade 1 endometrioid adenocarcinoma and confirmed the absence of myometrial invasion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b
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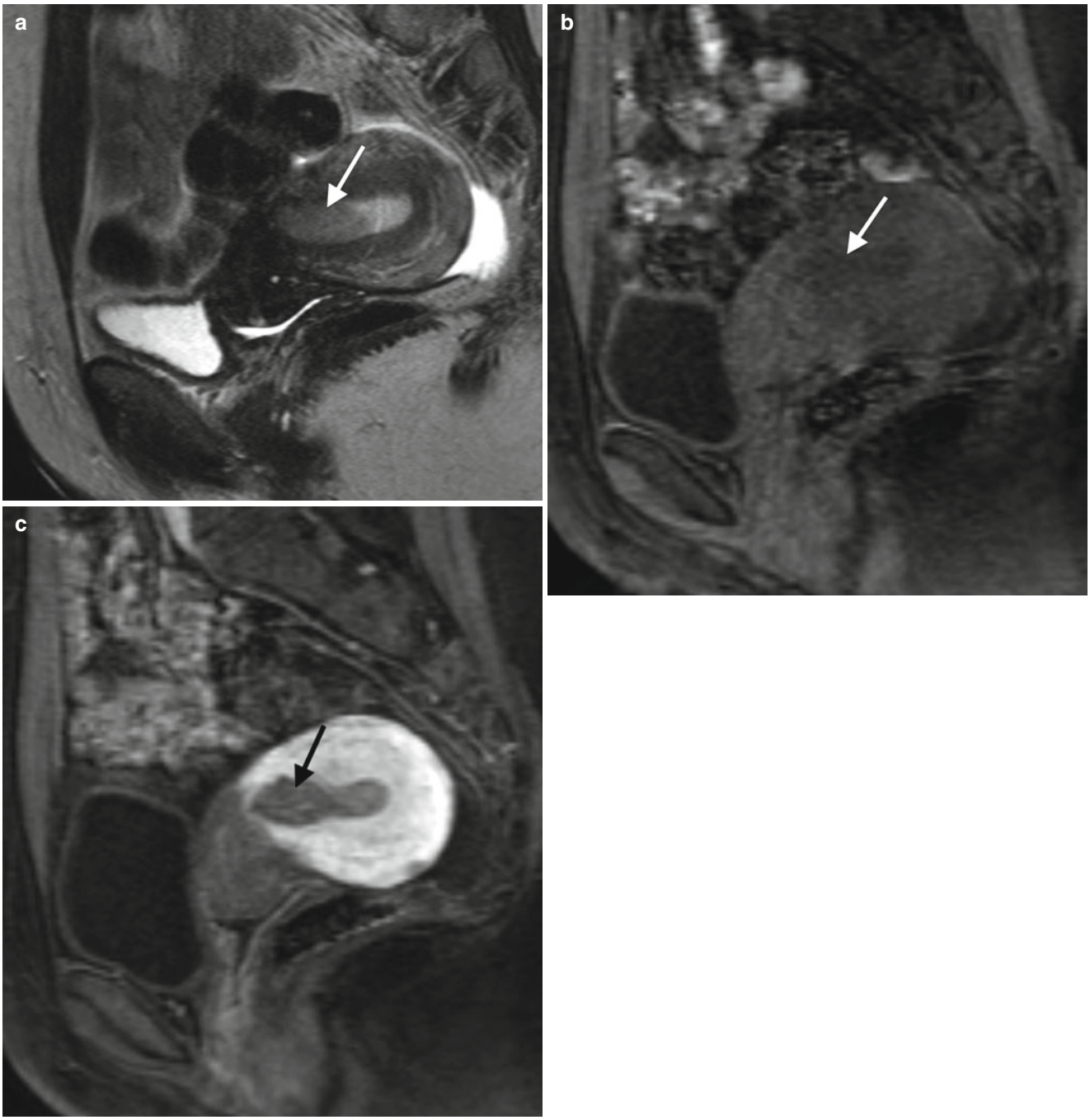


Fig. 2.11 FIGO stage IA endometrial cancer in a 37-year-old woman with vaginal bleeding between menstrual periods. A sagittal T2-weighted MR image (**a**) and fat-suppressed sagittal T1-weighted images before (**b**) and after (**c**) intravenous gadolinium demonstrate an endometrial mass with minimal irregularity at the endometrium-myometrium interface, probably representing superficial myometrial invasion. Pathology showed endometrioid adenocarcinoma

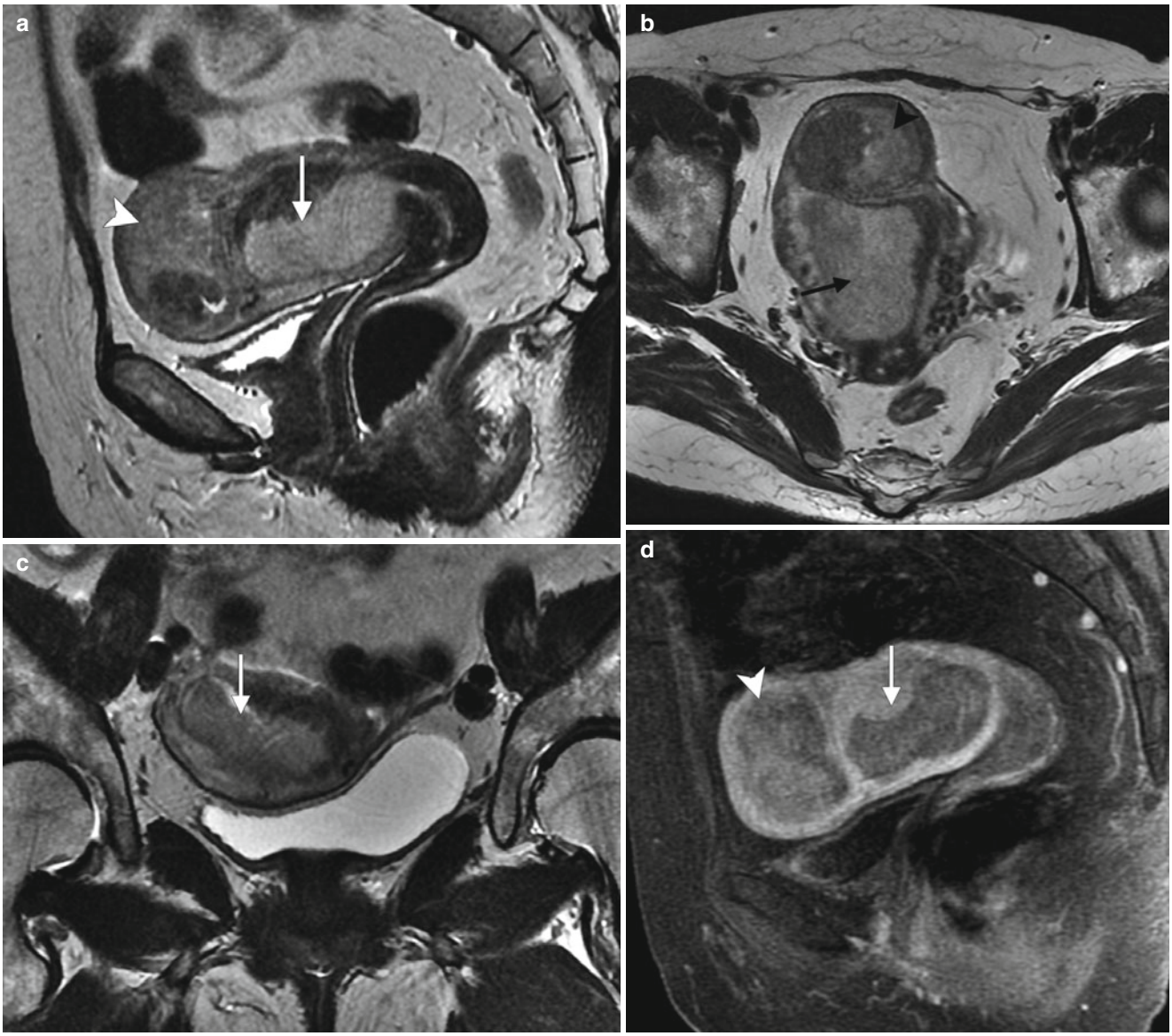


Fig. 2.12 FIGO stage IB endometrial cancer in a 66-year-old woman presenting with postmenopausal vaginal bleeding. Sagittal (**a**), axial (**b**), and coronal (**c**) T2-weighted MR images and a sagittal, fat-suppressed T1-weighted image following intravenous gadolinium (**d**) demonstrate a soft tissue mass centered on the endometrial cavity (*arrows*) with deep (>50 %) myometrial invasion. A benign leiomyoma (*arrowheads*) is also shown. Pathology was consistent with endometrioid adenocarcinoma

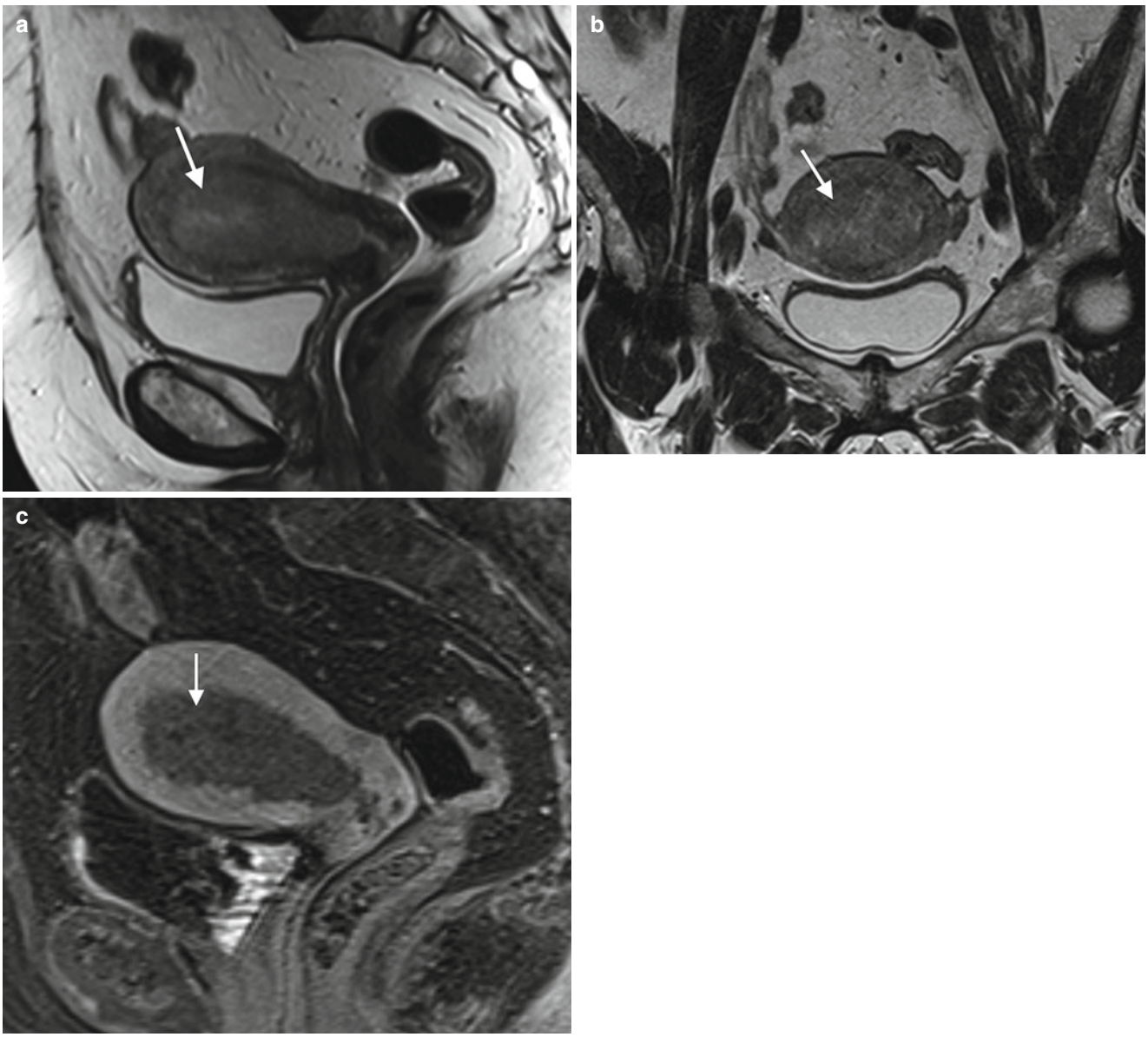


Fig. 2.13 FIGO stage IB endometrial cancer in a 66-year-old woman with postmenopausal vaginal bleeding. Axial (**a**) and oblique coronal (**b**) T2-weighted MR images and a sagittal, fat-suppressed T1-weighted image following intravenous gadolinium (**c**) demonstrate an endometrial soft tissue mass (*arrows*) with deep (>50 %) myometrial invasion. Pathology showed endometrioid adenocarcinoma

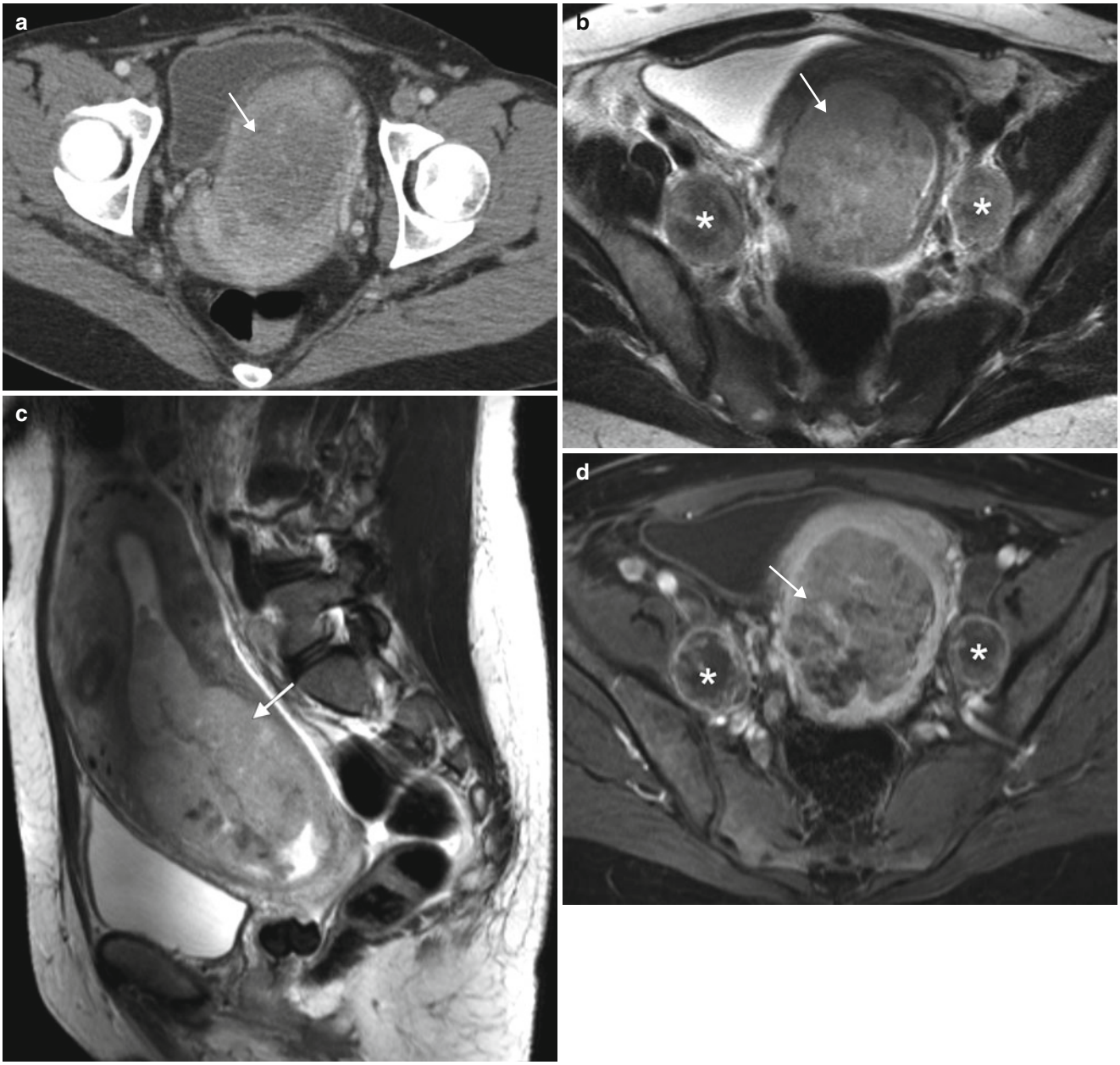
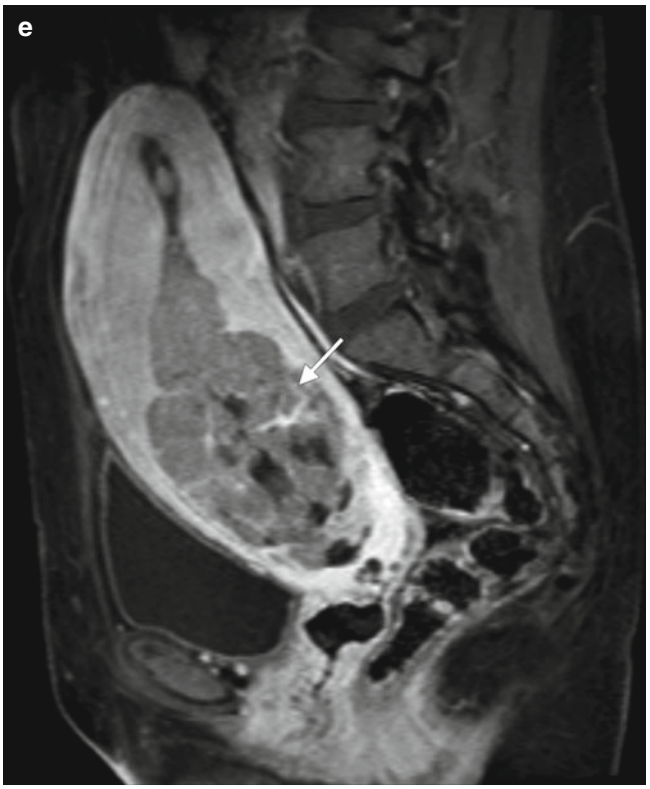


Fig. 2.14 51-year-old woman presenting with vaginal discharge and crampy abdominal pain. An axial, contrast-enhanced CT scan (**a**) demonstrated a heterogeneously enhancing uterine mass. Axial (**b**) and sagittal (**c**) T2-weighted MR images and fat-suppressed axial (**d**) and sagittal (**e**) T1-weighted images following intravenous gadolinium demonstrate a heterogeneously enhancing endometrial mass with deep myometrial invasion (>50 %) (*arrows*). Bilateral metastatic pelvic lymph node involvement is also shown (*asterisks*). Pathology showed an undifferentiated carcinoma with a minor, well-differentiated endometrioid adenocarcinoma component



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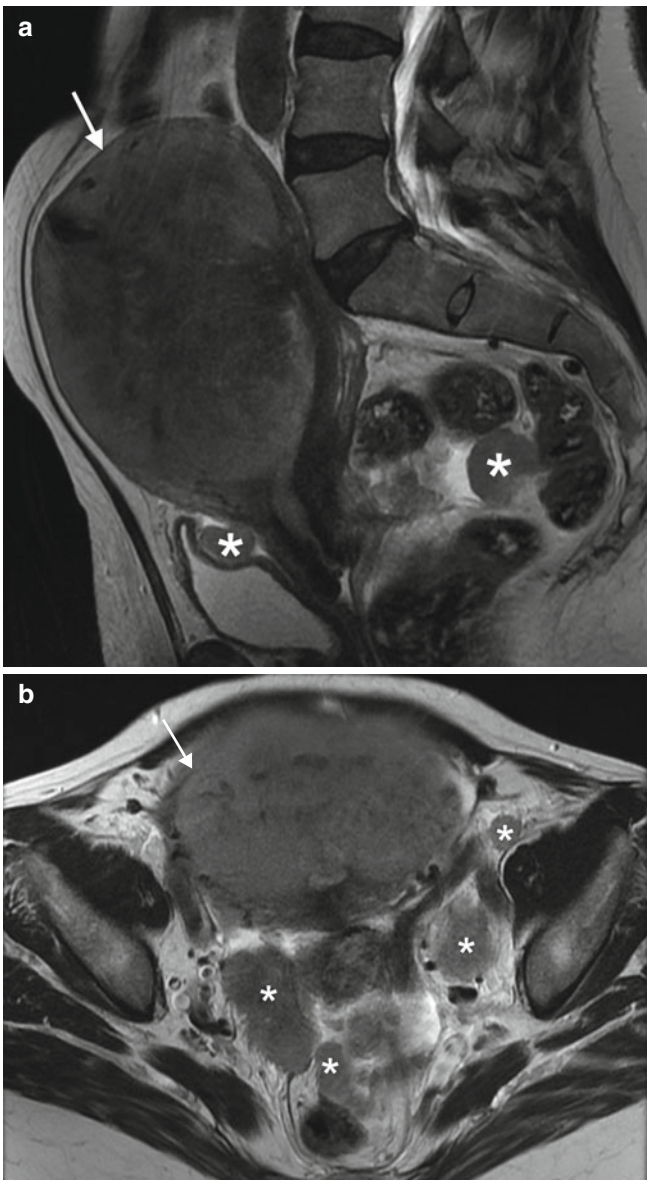
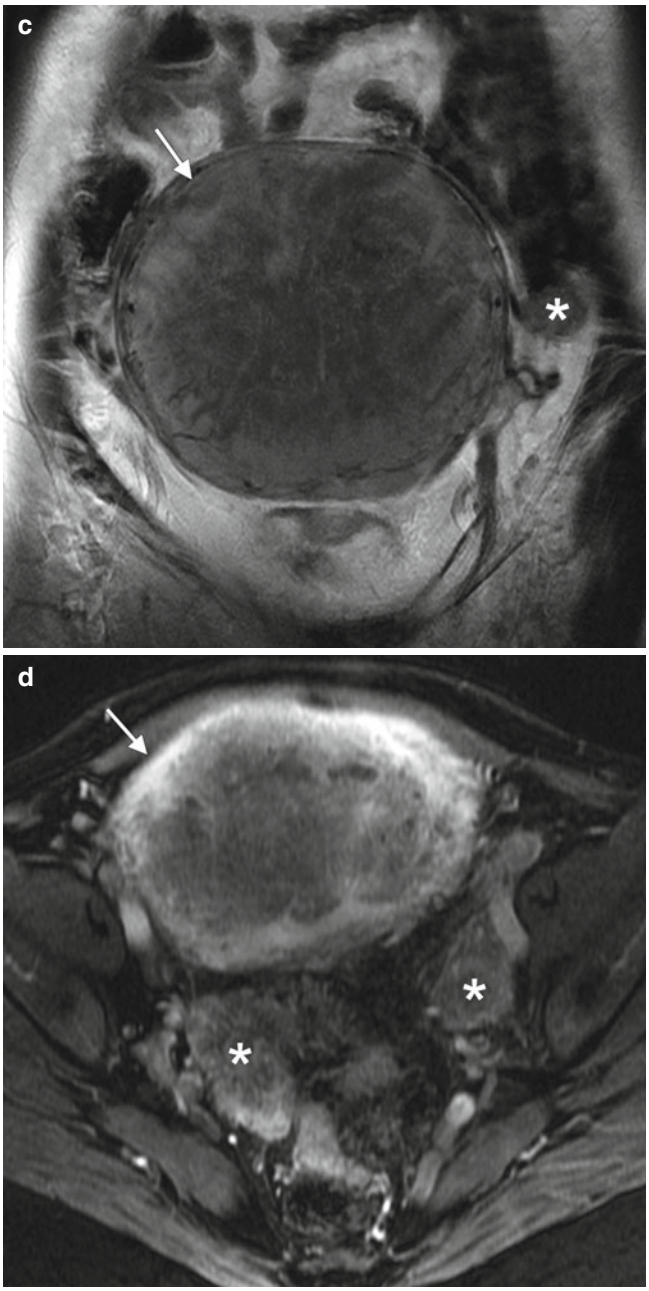


Fig. 2.15 FIGO stage III endometrial cancer in a 52-year-old woman complaining of increasing abdominal girth and irregular perimenopausal vaginal bleeding. Sagittal (**a**), axial (**b**), and coronal (**c**) T2-weighted MR images and a sagittal, fat-suppressed T1-weighted image following intravenous gadolinium (**d**) demonstrate a large, heterogeneously enhancing endometrial mass extending to the serosa (*arrows*). Bilateral metastatic involvement of pelvic nodes is also present (*asterisks*). Pathology was reported as undifferentiated endometrial adenocarcinoma



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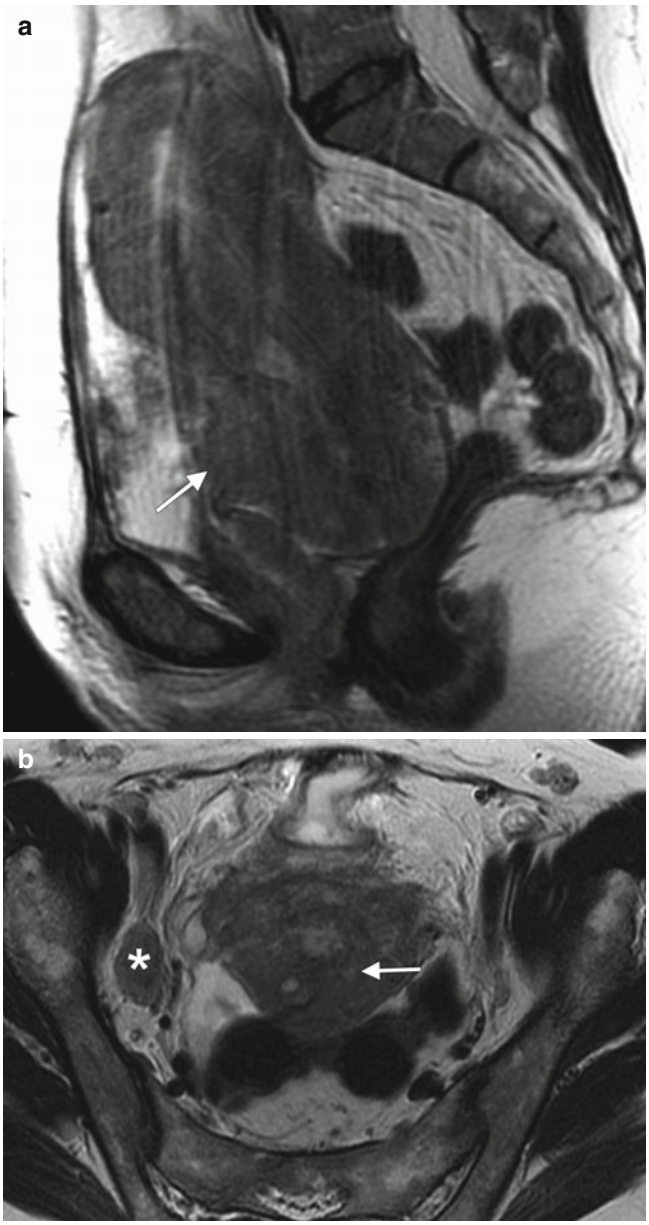


Fig. 2.16 FIGO stage III endometrial cancer in a 49-year-old woman with menorrhagia. Sagittal (**a**) and axial (**b**) T2-weighted MR images and an axial, fat-suppressed T1-weighted image following intravenous gadolinium (**c**) demonstrate a heterogeneous endometrial mass (*arrows*) with extension beyond the uterine serosa and ovarian metastasis (*asterisks*). An axial T1-weighted MR image (**d**) shows a T1-hypointense lesion (*arrowhead*) suspicious for metastasis

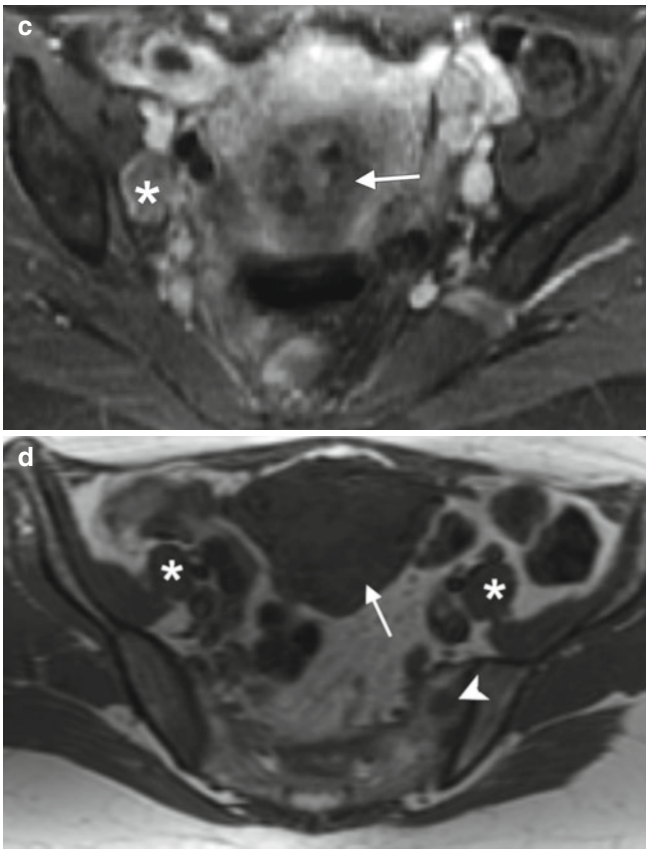


Fig. 2.16 (continued)

2.4 Uterine Sarcomas

Uterine sarcomas are rare forms of tumors arising from the mesenchymal or stromal elements of the uterus. The most common types of uterine sarcomas are leiomyosarcomas, carcinosarcomas (also called malignant mixed müllerian tumors [MMMTs]) and endometrial stromal sarcomas. They are aggressive tumors, and even when detected early in the disease course, they have a worse prognosis than the much more common epithelial endometrial carcinomas. Overall 5-year survival for uterine sarcomas ranges from 17.5 to 54.7 % [8], compared with 5-year survival rates of up to 83 % for endometrial cancer [1]. For stage I tumors alone, the 5-year survival rate for leiomyosarcoma is only about 51 %, compared with 96 % for endometrial cancer [1, 9].

Carcinosarcomas are staged according to the 2009 FIGO staging criteria for endometrial carcinomas. For the first time, the 2009 FIGO staging system provided separate staging criteria for leiomyosarcomas and endometrial stromal sarcomas and adenosarcomas. The main differences from the staging of epithelial endometrial cancers include the use of tumor size (as opposed to depth of myometrial invasion) for defining stage I disease, replacing cervical involvement with extrauterine extension for defining stage II disease, and replacing serosal and vaginal involvement with involvement of the omentum and other abdominal tissues for defining stage IIIA and IIIB disease.

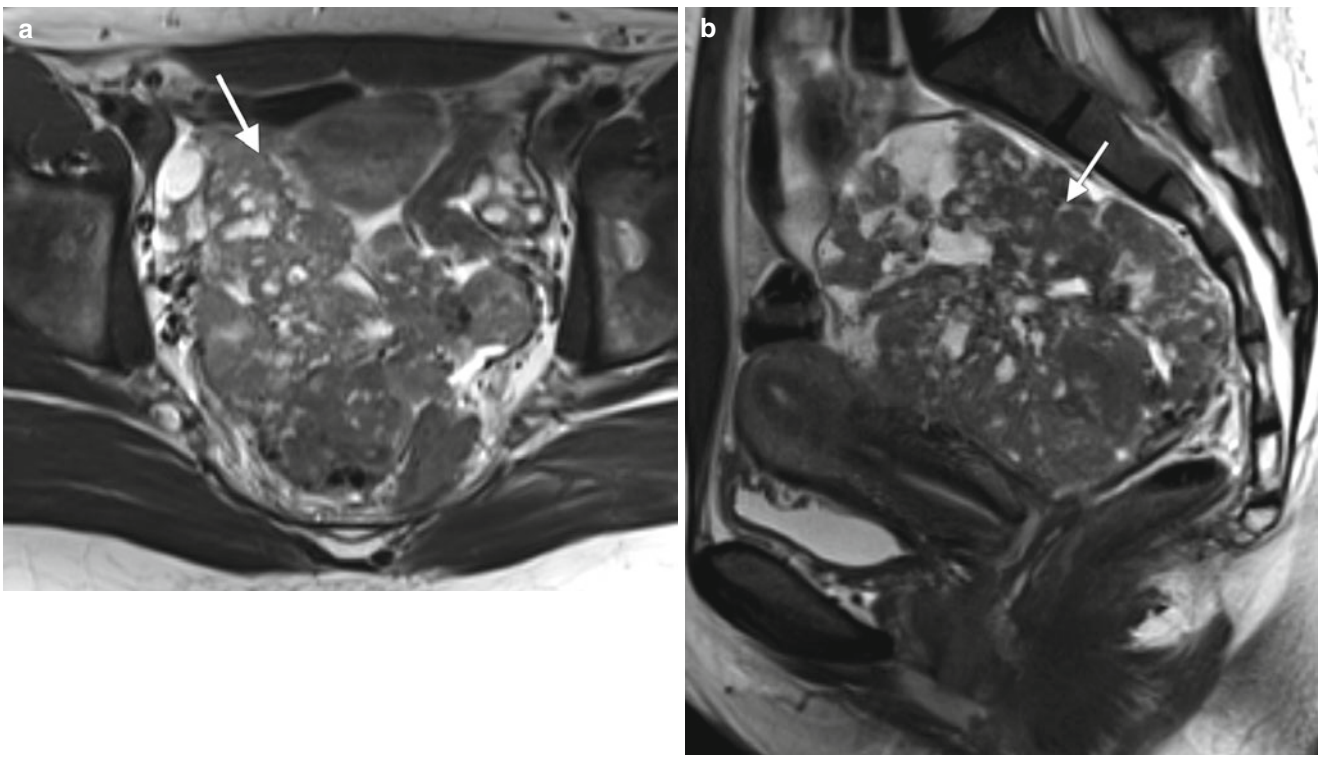
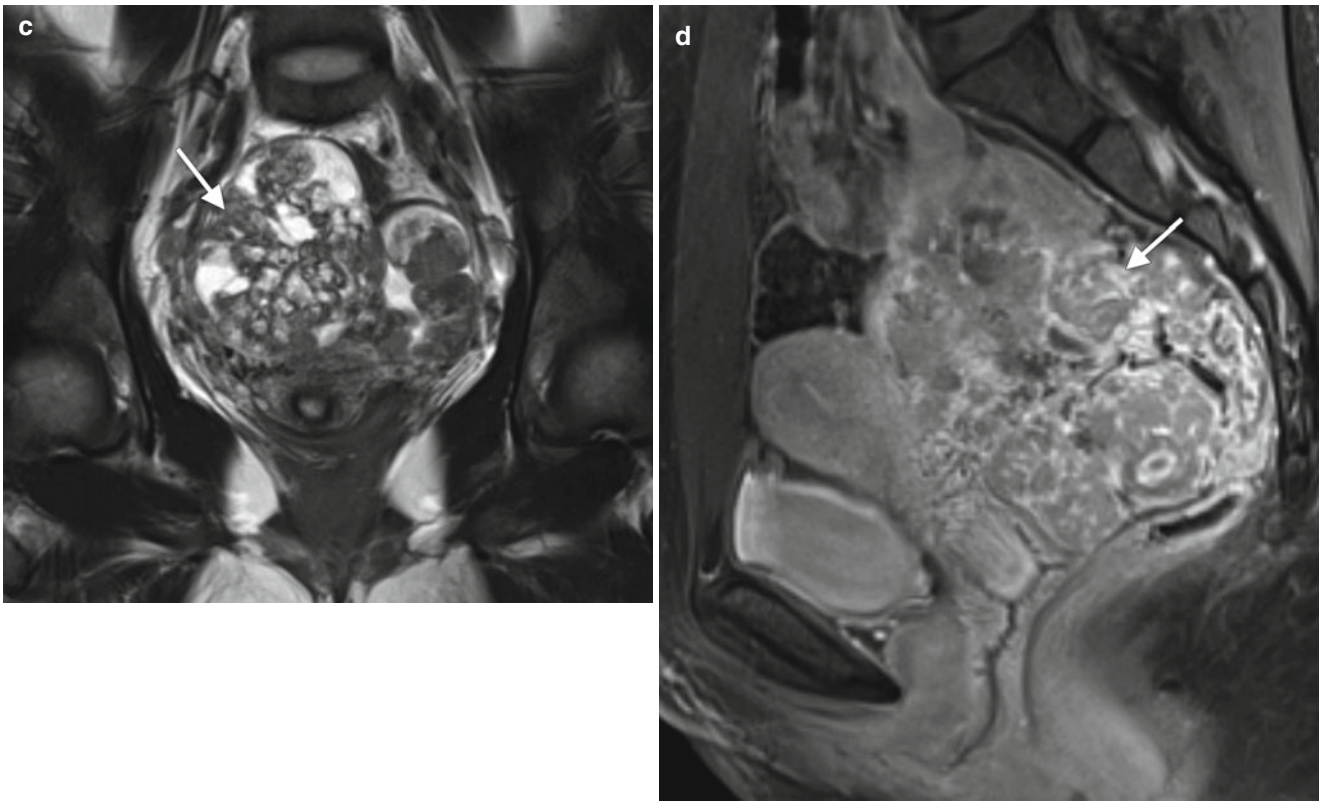


Fig. 2.17 High-grade leiomyosarcoma in a 37-year-old woman with a history of menorrhagia and multiple submucosal uterine leiomyomas resected hysteroscopically 3 years earlier. Axial (**a**), sagittal (**b**), and coronal (**c**) T2-weighted MR images and a sagittal, fat-suppressed T1-weighted image following intravenous gadolinium (**d**) demonstrate a loculated, heterogeneous, partially necrotic pelvic mass arising from the posterior aspect of the uterus and displacing the rectum posteriorly



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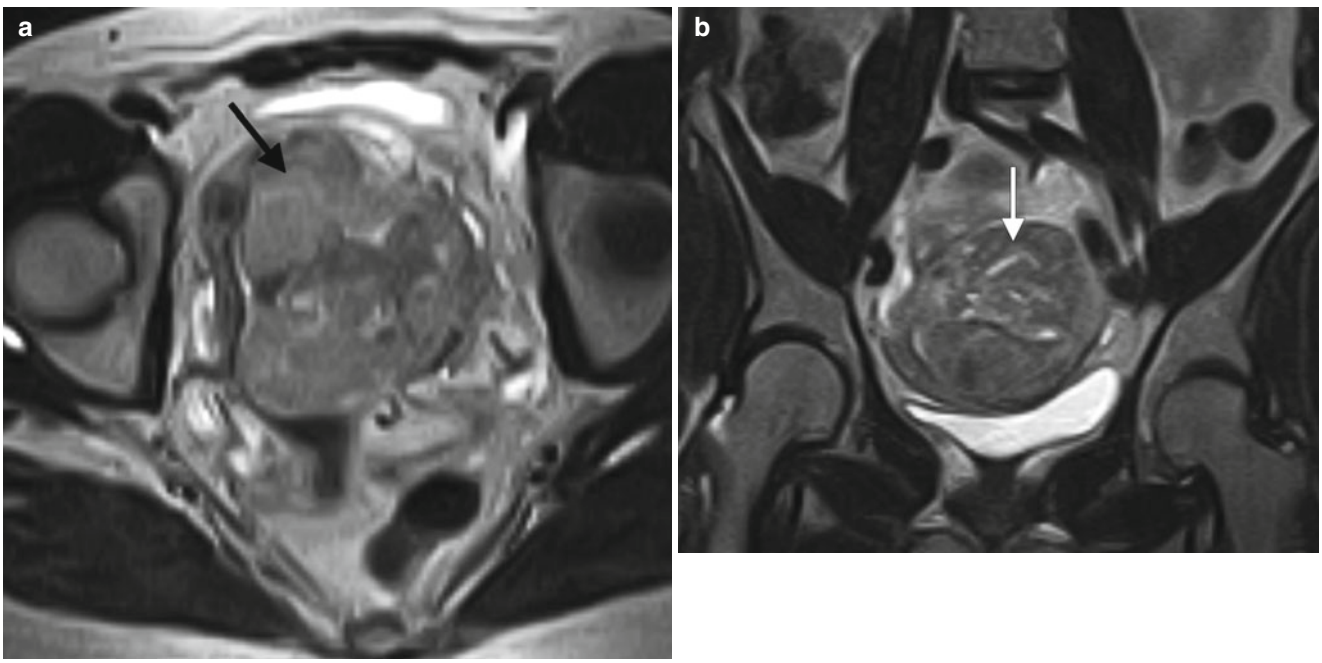
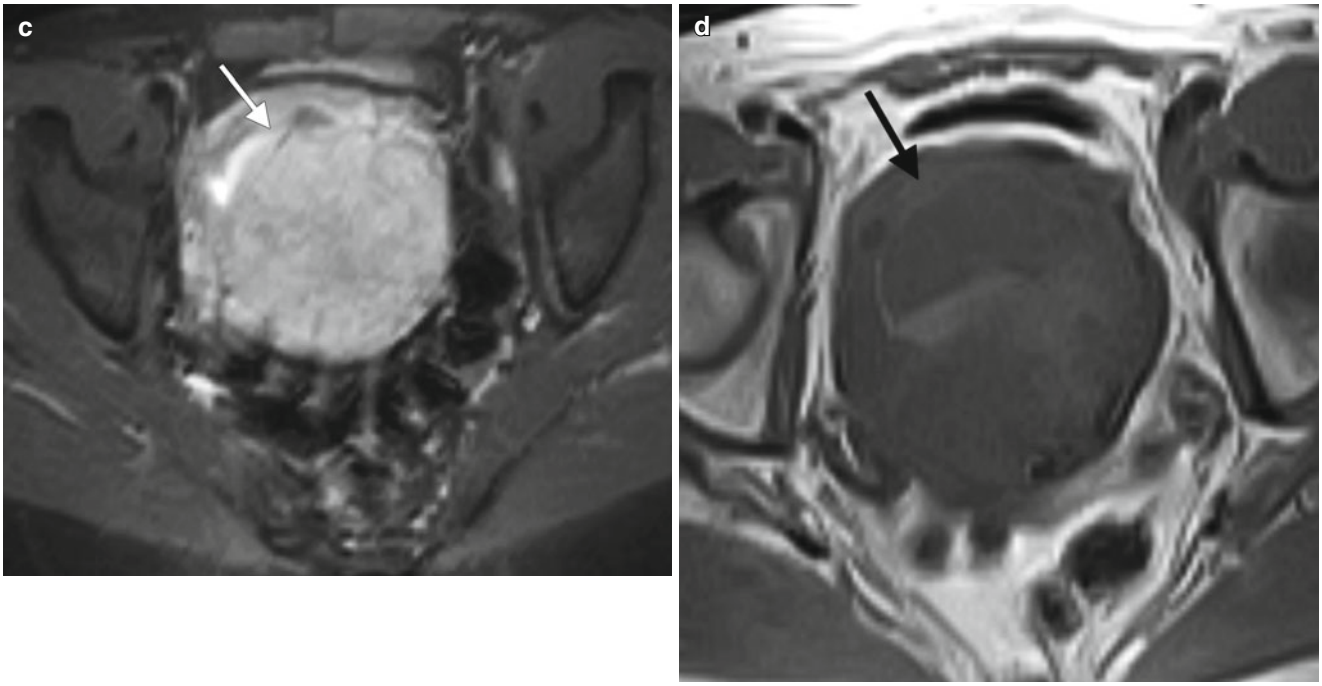


Fig. 2.18 High-grade epithelioid leiomyosarcoma in a 53-year-old woman with pelvic pain. Axial (**a**) and coronal (**b**) T2-weighted MR images, an axial fat-suppressed T1-weighted image following intravenous gadolinium (**c**), and an axial T1-weighted image (**d**) demonstrate a heterogeneously enhancing myometrial mass (*arrows*). Pathology showed a high-grade epithelioid leiomyosarcoma



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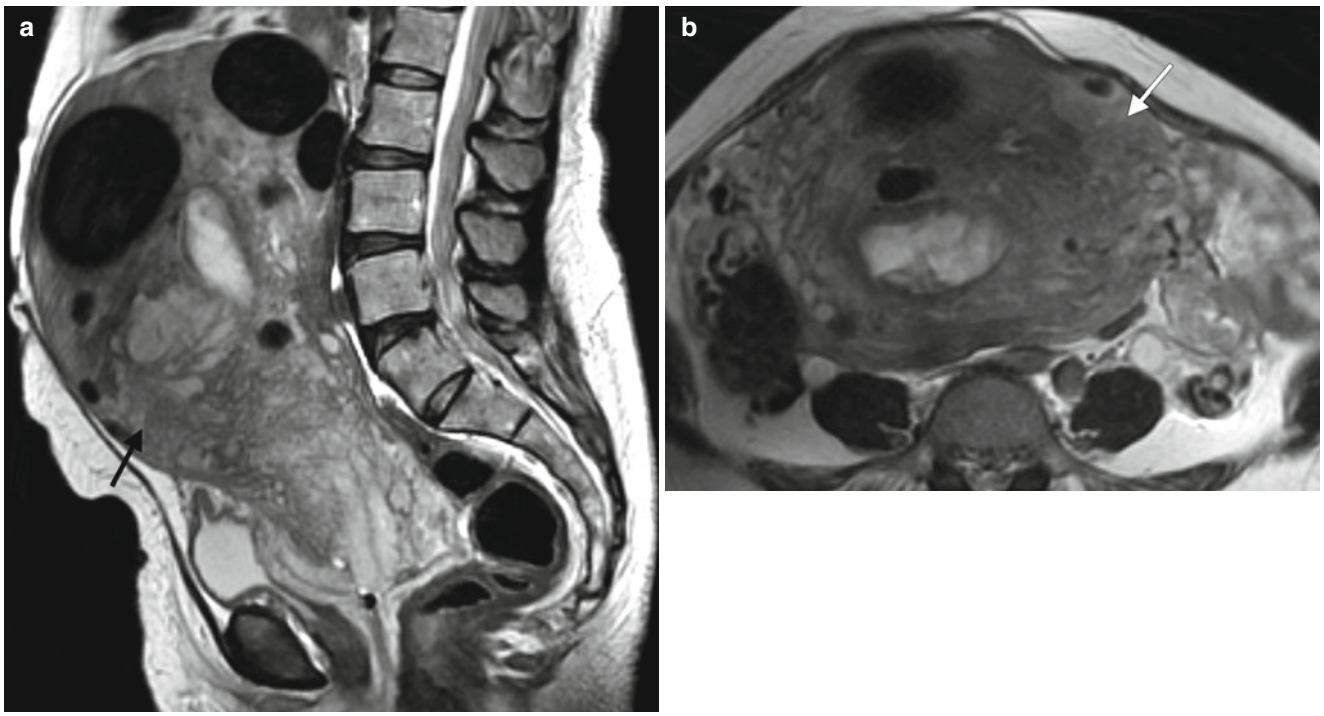

Fig. 2.19 Endometrial stromal sarcoma in a 58-year-old woman with postmenopausal vaginal bleeding. Sagittal (**a**) and axial (**b**) T2-weighted MR images demonstrate a large, heterogeneous mass (*arrows*) with mixed solid and cystic components involving the endometrium and myometrium and extending beyond the uterine serosa, with involvement of both ovaries. Pathology showed an endometrial stromal sarcoma

2.5 Endometrial Cancer Treatment and the Role of Lymphadenectomy

Endometrial cancer is staged and treated surgically. Surgery includes radical hysterectomy and bilateral salpingo-oophorectomy. Lymphadenectomy for early-stage (stage I) endometrial cancer remains controversial. Two large, prospective, multicenter studies investigated whether pelvic lymphadenectomy could improve the survival of women with early-stage endometrial cancer. Both studies reported no benefit in overall or recurrence-free survival in the patients randomized to lymphadenectomy [10, 11]. The recent SEPAL study (Survival Effect of Para-aortic Lymphadenectomy in endometrial cancer) showed that pelvic and para-aortic lymphadenectomy improves outcome in patients with an intermediate or high risk of recurrent disease [12]. Adjuvant treatment with chemotherapy, radiotherapy, or both is performed for women with stage III and IV endometrial cancer, although certain subgroups of women with earlier-stage disease may also benefit [13].

Endometrial cancers presenting in premenopausal women (about 20 % of all endometrial cancers) require special consideration. Some advocate ovarian preservation for this patient population in order to prevent surgical menopause [13]. However, these patients are at risk of synchronous and metachronous ovarian neoplasms. For women who wish to retain fertility, uterine preservation by medical treatment with a progestational agent can also be considered [13].

2.6 Endometrial Cancer Recurrence

The most common site of endometrial cancer recurrence is the vaginal cuff. The treatment of choice for women who have a relapse at the vaginal cuff after surgery is radiation, with 2-year survival after an isolated recurrence at the vaginal cuff being as high as 75 % [14, 15]. However, patients with recurrent endometrial cancer constitute a highly heterogeneous population that includes women presenting with widespread disease (in whom palliation constitutes the mainstay of treatment) in addition to those presenting with isolated vaginal cuff recurrences. As such, treatment is highly individualized. Surgery, radiation, chemotherapy, and hormonal therapy are all used for recurrent endometrial cancer.

The typical patient with endometrial cancer is a postmenopausal woman presenting with vaginal bleeding, although up to 20 % of cases occur in premenopausal women. The hallmark of endometrial cancer on imaging is thickening of the endometrial stripe. Endometrial cancer is staged and treated surgically. Imaging provides important prognostic information, such as depth of myometrial invasion by tumor and lymph node involvement, and thus contributes to an individualized treatment approach.

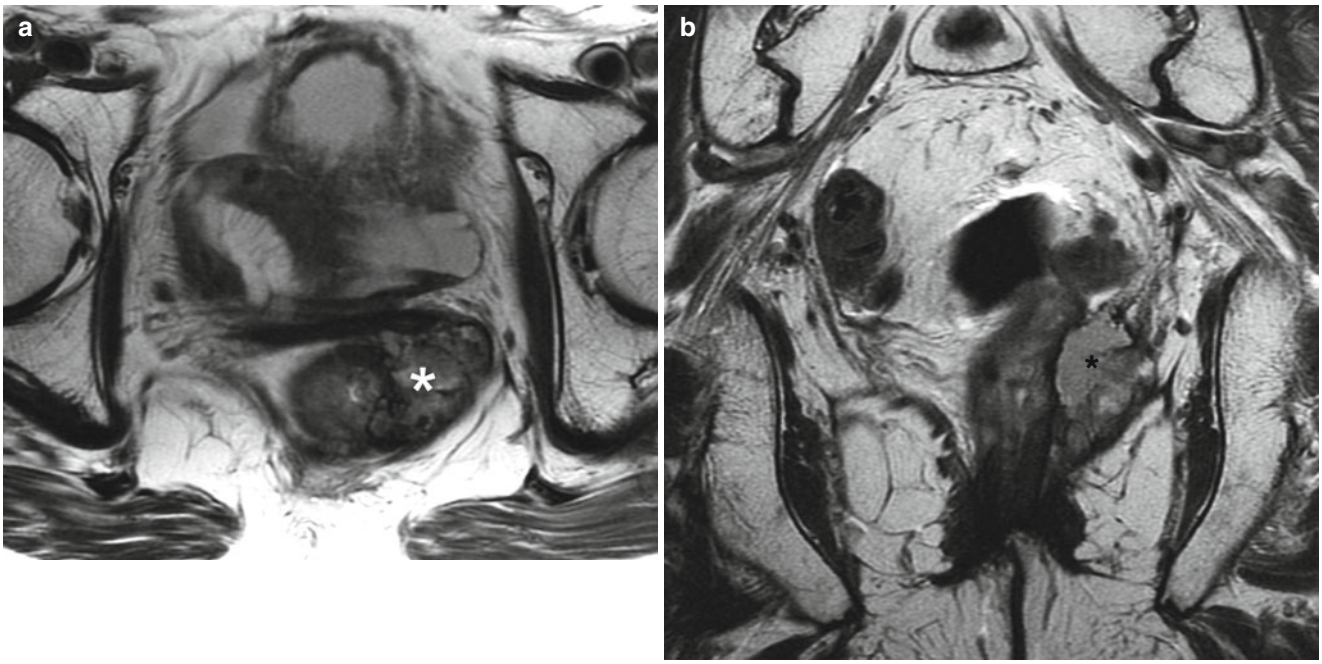

Fig. 2.20 This 72-year-old woman had a history of endometrioid endometrial adenocarcinoma treated with radical hysterectomy, bilateral salpingo-oophorectomy, and adjuvant chemotherapy 10 years earlier. Axial (**a**), coronal (**b**), and sagittal (**c**) T2-weighted MR images and an axial, fat-suppressed T1-weighted image following intravenous gadolinium (**d**) demonstrate a partially necrotic left pelvic tumor (*asterisks*) abutting the vagina with probable invasion of the rectal wall and left levator ani muscle. The soft tissue demonstrates hypermetabolic activity (*arrows*) on a fused FDG-PET scan of the pelvis (**e**). Axial (**f**) and coronal (**g**) contrast-enhanced CT scans of the upper abdomen demonstrate a perihepatic implant (*arrowheads*)

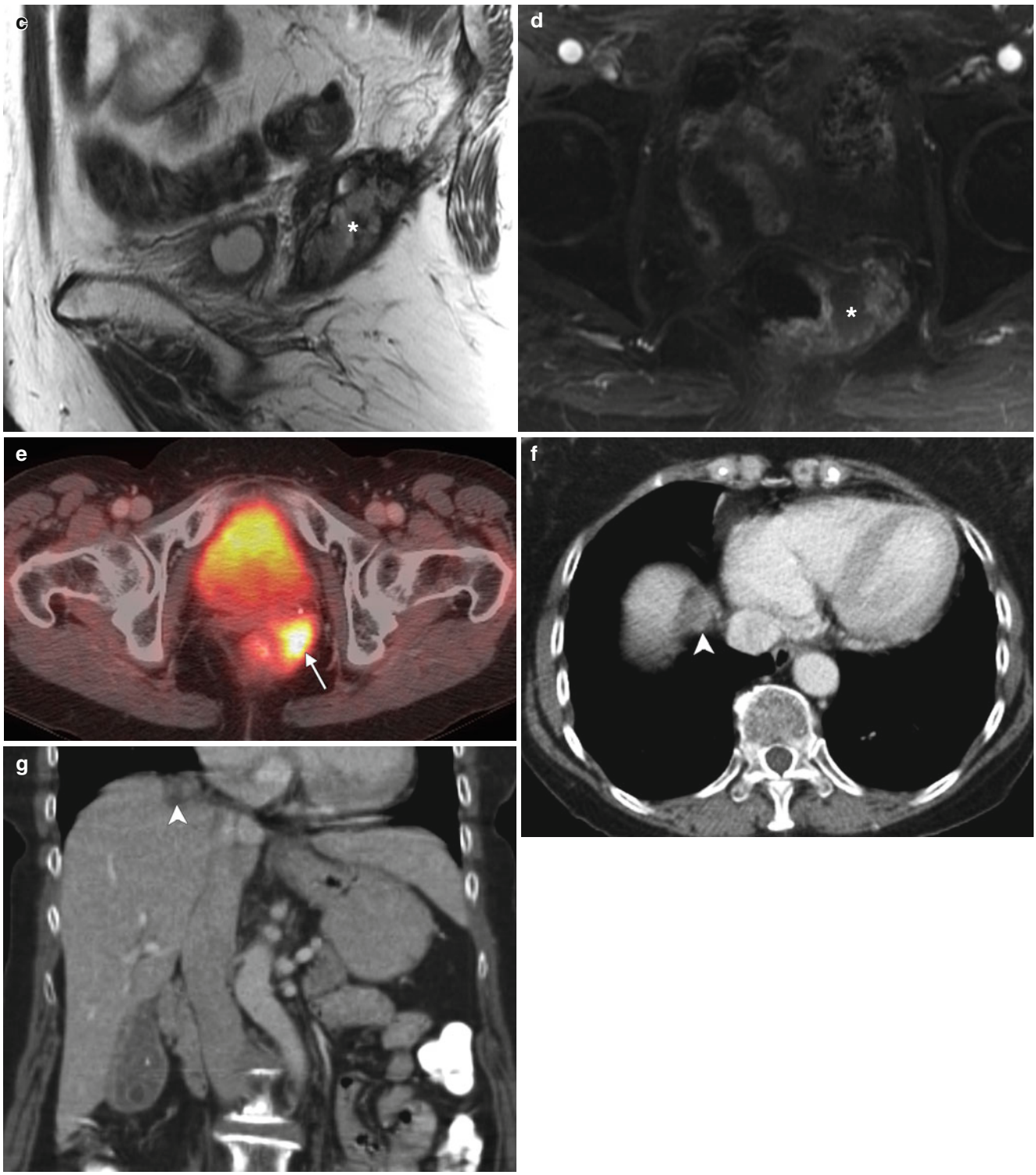

Fig. 2.20 (continued)

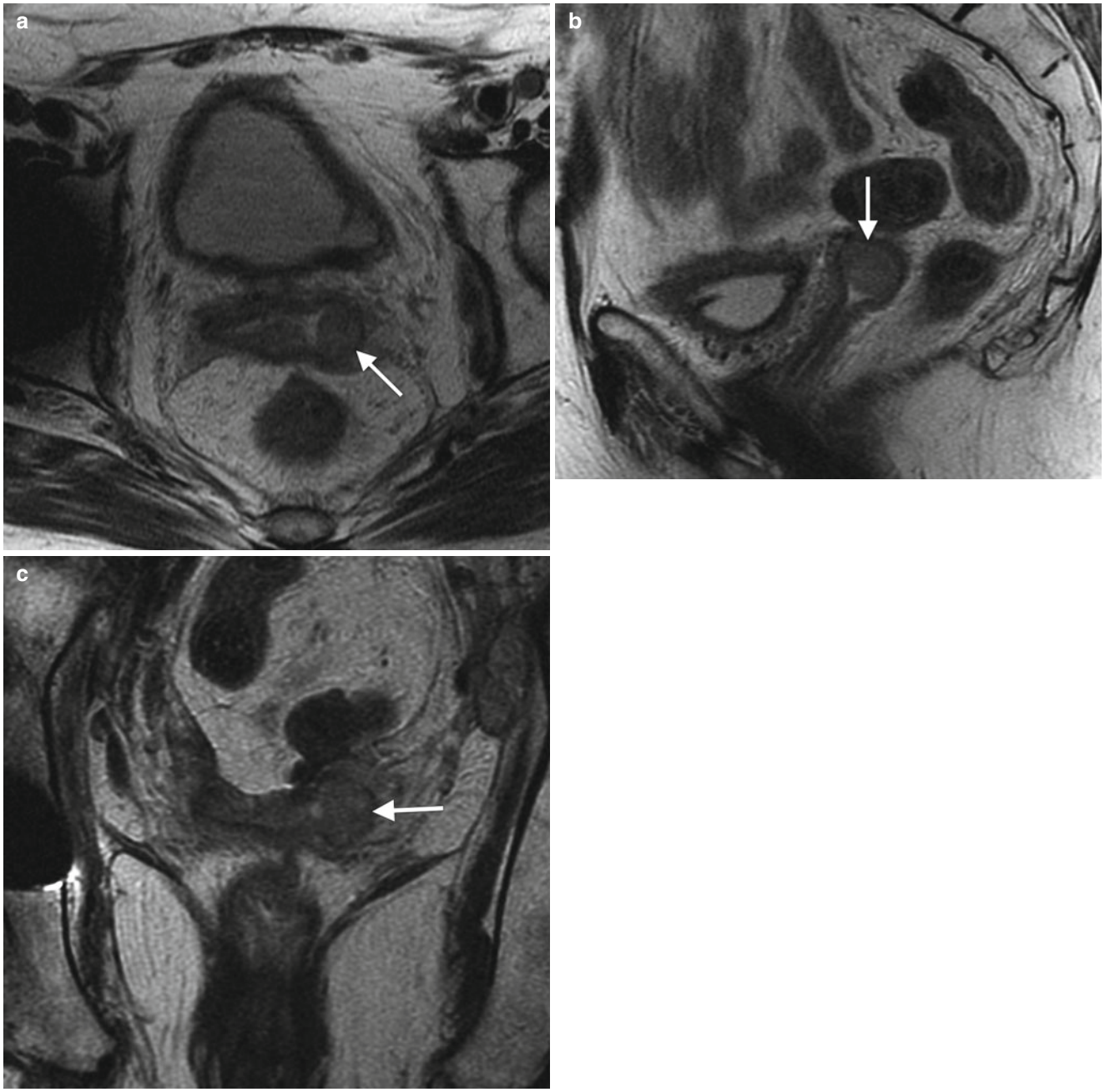

Fig. 2.21 This 68-year-old woman had a history of clear cell adenocarcinoma of the endometrium, which was treated with adjuvant chemotherapy followed by radical hysterectomy and bilateral salpingo-oophorectomy 2 years earlier. Axial (**a**), sagittal (**b**), and coronal (**c**) T2-weighted MR images demonstrate a soft tissue mass in the left aspect of the vaginal cuff (*arrows*) consistent with cancer recurrence

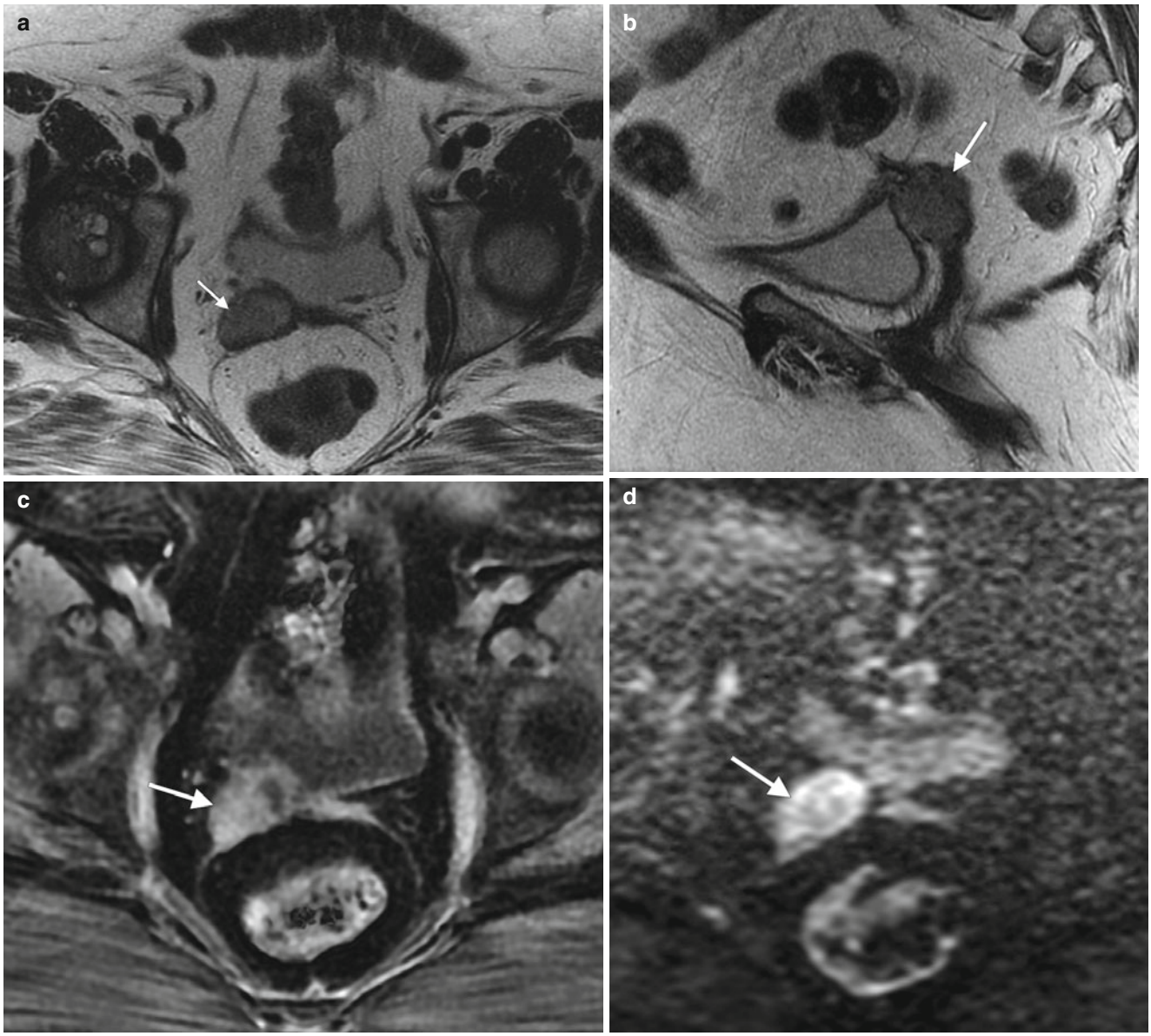

Fig. 2.22 This 53-year-old woman had a history of stage IA endometrioid adenocarcinoma of the endometrium, which was treated with radical hysterectomy and bilateral salpingo-oophorectomy 2 years earlier. Axial (**a**) and sagittal (**b**) T2-weighted MR images, an axial, fat-suppressed T1-weighted image following intravenous gadolinium (**c**), and an axial diffusion-weighted MR image (b = 300) (**d**) demonstrate a soft tissue mass in the right side of the vaginal cuff (*arrows*) consistent with cancer recurrence. The tumor abuts the posterior bladder wall and anterior mesorectal fascia

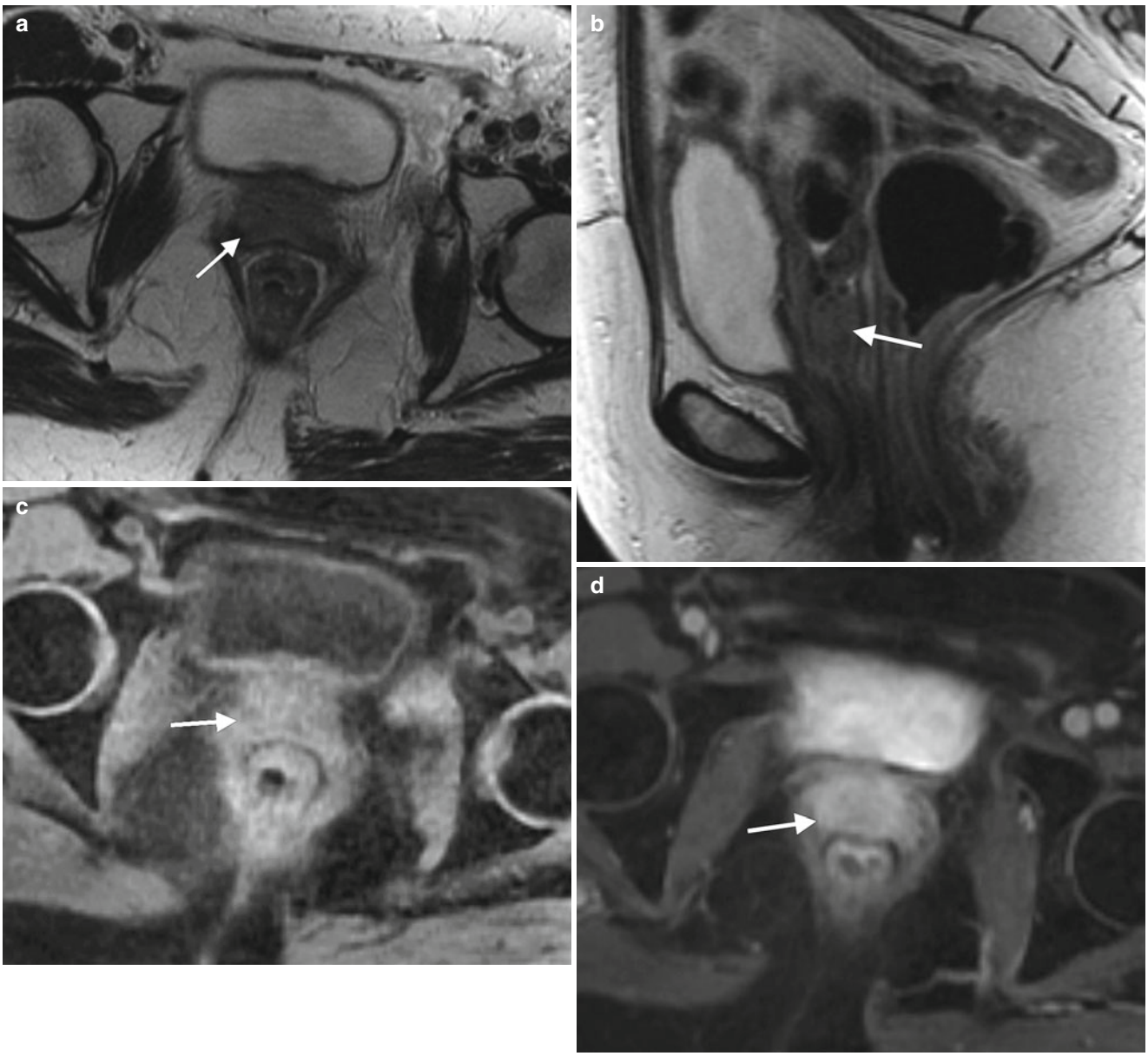

Fig. 2.23 This 59-year-old woman had a history of stage IIIC endometrioid adenocarcinoma of the endometrium, treated with radical hysterectomy and bilateral salpingo-oophorectomy 9 months earlier. Axial (**a**) and sagittal (**b**) T2-weighted MR images and axial, fat-suppressed T1-weighted images before (**c**) and after (**d**) intravenous gadolinium demonstrate a soft tissue mass in the vaginal cuff (*arrows*) consistent with cancer recurrence

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